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Frequencies and ethnic distribution of ABO/Rh blood groups in China: a population-based cross-sectional study

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Abbreviations: Rh, rhesus; NFPHEP, National Free Preconception Health Examination Project; EQA, external quality assessment; CI, confidence interval.

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Abstract

Objectives ABO and rhesus (Rh) blood groups play a vital role in blood transfusion safety and clinical practice. The distribution of ABO/Rh blood groups varies throughout the world. Previous evidence was primarily obtained from blood donors. There are limited data on the frequencies and ethnic distribution of ABO/Rh blood groups in the general population, especially in Asian populations.

Design A population-based cross-sectional study.

Setting Data was from the National Free Preconception Health Examination Project (NFPHEP) in which participants from 220 counties of 31 provinces in China.

Participants 3 832 034 participants aged 21 to 49 years who engaged in the NFPHEP between January 2010 and December 2012 were included, after excluding participants without ABO/Rh blood typing.

Outcome Measures The proportions of ABO and Rh blood groups among different ethnic groups were calculated.

Results The proportions of ABO/Rh blood groups were significantly different among nine ethnic groups (P<0.001). Compared with other ethnic groups, Yi ethnic group was with higher proportion of A phenotype (33.95%), while Manchu (33.69%) and Mongolian (33.27%) ethnic groups were with higher proportions of B phenotype. Zhuang ethnic group was with the highest proportion of O phenotype (41.81%), followed by Miao ethnic group (37.71%). Compared with other ethnic groups, the proportions of AB phenotype were higher in the Uygur ethnic group (10.60%) but lower in the Zhuang ethnic group (5.5%). Meanwhile, the proportions of Rh (D) negativity were higher in the Uygur (3.33%) than in the Mongolian (0.34%) and Manchu ethnic groups (0.36%). The proportion of ORh- blood group was higher in the Uygur (0.84%) than in other ethnic groups (0.08%-0.39%, P<0.001).

Conclusion ABO and rhesus blood phenotypes varied across different ethnic groups in China. The diversity on distribution of ABO/Rh blood groups in different ethnic groups should be considered when making rational and evidence-based strategies on blood collection and management.

Strengths and limitations of this study

- To the best of our knowledge, this is the largest population-based study of ABO/Rh distribution in different ethnic groups among the general population in an Asian country.
- Major limitation of the study was no further laboratory data on subtypes of ABO blood groups (e.g. A1, A2, A3, Aw, Ax, Ael).
- We did not analyze all the ethnic minorities in China as lack of relative information.
- Willingness and histories of blood donation of participants were not investigated that we could not provide specific evidence on donor recruitment.

Introduction

ABO and rhesus (Rh) blood groups, the most well-known blood group systems, play a vital role in blood transfusion safety and clinical practice. Blood groups are also thought to be linked with disease susceptibility[1, 2]. The distribution of ABO/Rh blood groups varies throughout the world.[3-5] Previous studies have found the percentage of blood group O to be 46.6% in the United States[3], 34% in China[4], 49.10% in Mauritanian[5], 38.9% in Sweden[6] and 42.3% in Denmark[6]. The proportions of those with Rh-D negative blood have been reported to be 14.6% in the United States[3], 17.9% in Sweden and Denmark[6] and 0.4%-1.0% in China[4]. And it also varies among different race or ethnic populations.[3, 5, 7] In the United States, the percentages of group O vary from 39.8% in Asian donors to 56.5% in Hispanic donors, and the proportions of Rh (D) negativity vary from 1.7% in Asian donors to 17.3% in White non-Hispanic donors.[3] Data regarding the distribution of ABO/Rh blood group was primarily obtained from blood donors in the previous studies, while little from general population.

China houses more than 20% of the world's population, and its blood supply has a potential effect on the global community.[8] Social-economic development and increased health care coverage have caused a sharp increase in the clinical demand for blood and its products in China[9]. Despite a steady increase in total blood collections and voluntary non-remunerated blood donors, China continues to face many challenges with its blood donation system.[10] The country's donation rate remains relatively low at 9‰, and over 60% of donors are first-time donors.[10] Basic information on the frequencies and ethnic distribution of ABO/Rh blood groups in the general population is crucial to make rational and evidence-based strategies on blood collection and management. However, studies that focused on the frequencies and ethnic distribution of ABO/Rh blood groups in the general population have been scarce in China.

We did a large population-based study to investigate the distribution of ABO and Rh (D) blood groups in different ethnic groups in the Chinese general population, in order to provide reliable data for better development of rational strategies on blood collection and management.

Materials and methods

Study design and data source

We did a nationwide population-based, cross-sectional study using data from the National Free Preconception Health Examination Project (NFPHEP). The NFPHEP was a national health check-up program aiming to provide free preconception health examinations and counseling services for married couples who were preparing for pregnancy. It was launched by the Chinese National Health and Family Planning Commission and the Ministry of Finance in 2010. Project-related design and implementation have been described previously[11-14]. This study was approved by the Institutional Review Board of the Chinese Association of Maternal and Child Health Studies. All participants were provided with written informed consent forms before enrollment.

From January 1, 2010, to December 31, 2012, there were 4 150 214 participants (including 2 120 131 women and 2 030 083 men) aged 21–49 years from 220 counties in 31 provinces enrolled in the NFPHEP, covering 86.06% of the target population[15]. 318 180 (7.67%) participants who did not undergo ABO/Rh blood typing were excluded from this study. Finally, 3 832 034 (2.33%) of the enrolled participants were included for analysis.

Questionnaire and laboratory testing

Basic information was collected by trained local health workers from all participants in the

NFPHEP, using a standardized questionnaire, including gender, age, educational level, occupation, ethnicity and address of residence. During physical examination, trained local health workers collected blood samples from all participants and immediately sent to local laboratories. Testing for both ABO and rhesus blood groupings was performed simultaneously with reagents (anti-A, anti-B, anti-AB, and anti-D). Red blood cell agglutination method was used for analysis of blood typing. The National Center of Clinical Laboratories for Quality Inspection and Detection did the biannual external quality assessment (EQA) for quality control.

In this study, we divided participants into nine groups with larger size of population according to their ethnic groups, including Han, Uygur, Zhuang, Manchu, Miao, Yi, Mongolian, Hui and others.

Statistical analysis

We used proportions to describe the distribution of gender, age groups, ethnicity and other socio-demographic characteristics of participants. We used Chi-square test to compare the proportions of A, B, AB and O blood groups in different ethnic groups. And the Chi-square test was also used to compare the proportion of Rh (D) negative blood group among different ethnic groups. According to ABO phenotypes (A, B, AB, and O) and Rh phenotypes (Rh+ and Rh-), we then divided participants into eight blood groups, including ARh+, ARh-, BRh+, BRh-, ABRh+, ABRh-, ORh+ and ORh- blood groups. We used Chi-square test to compare the distribution of ABO/Rh phenotypes in different ethnic groups. All the analyses were done with SPSS version 18.0 (SPSS Inc., Chicago, IL, USA). Two-sided $p<0.05$ was considered to be statistically significant.

Results

Socio-demographic characteristics of study population

Of the 3 832 034 participants included in the study, 48.81% were male, 36.25% were older than 30 years, and 22.42% were living in the eastern areas of China. 3 473 527 (90.64%) participants were with Han ethnicity. The proportions of Uygur, Zhuang, Manchu, Miao, Yi, Mongolian and Hui ethnicity were 3.38%, 1.23%, 0.87%, 0.72%, 0.51%, 0.50% and 0.30%, respectively (table 1).

Distribution of ABO blood groups according to ethnicity

In the ABO blood system, blood group A (30.54%) appeared the most common phenotype, followed by O (30.38%), B (29.42%) and AB (9.66%). The proportions of A, B, O, AB blood groups were significantly different among nine ethnic groups (all $P<0.001$, table 2). Compared with other ethnic groups, Yi ethnic group was with higher proportion of A phenotype (33.95%), while Manchu (33.69%) and Mongolian (33.27%) ethnic groups were with higher proportion of B phenotype. Zhuang ethnic group was with the highest proportion of O phenotype (41.81%), followed by the Miao ethnic group (37.71%). And the proportions of AB phenotype were higher in the Uygur (10.60%) but lower in Zhuang ethnic group (5.5%). The distribution of ABO blood groups according to ethnicity was shown in figure 1 and figure 2.

Distribution of rhesus blood groups according to ethnicity

In the rhesus blood system, 98.98% of 3 832 034 participants were Rh (D) positive, while 1.02% were Rh (D) negative (table 3). The proportions of Rh (D) negative group were significantly different among nine ethnic groups ($\chi^2 = 7413.07$, $P<0.001$). Compared with other ethnic groups, the proportion of Rh (D) negativity appeared higher in Uygur (3.33%), while much lower in the Mongolian (0.34%) and Manchu ethnic groups (0.36%). The proportions of Rh (D) negative group according to ethnicity were shown in figure 3.

Distribution of ABO/Rh blood groups according to ethnicity

Compared with other ethnic groups, Yi ethnic group was with higher proportion of ARh+ blood group (33.58%), and Uygur ethnic group was with higher proportion of ARh- blood group (1.14%, all P<0.001). The proportion of ORh- blood group was higher in Uygur (0.84%) than in other ethnic groups (0.08%-0.39%, P<0.001). The proportion of ORh- blood group was higher in the Zhuang (41.67%) than in other ethnic groups (27.07%-37.51%, P<0.001). The proportions of ABRh+ blood group (10.28%) and ABRh- blood group (0.32%) were both higher in the Uygur than in other ethnic groups (all P<0.001). Distributions of ABO/Rh blood groups according to ethnicity were shown in figure 4 and table 4.

Discussion

ABO and rhesus blood phenotypes are hereditarily determined and vary widely across races/ethnicities and geographical boundaries.[3, 16] In this population-based study involving 3.8 million adults, we found that A phenotype (30.54%) was the most common phenotype, followed by O (30.38%), B (29.42%) and AB (9.66%). Guo et al.[3, 16] reported that the percentage of O phenotype was the highest (34.0%), followed by A (29.0%), B (27.2%), and AB (8.8%) by using data from 512 594 whole blood donations at the five blood centers in China from 2008 to 2009. Apecu et al.[17] conducted a retrospective study in 2014, using data of 25 504 voluntary blood donors from a regional blood bank in rural southwestern Uganda, and found that nearly half of the donors belonged to blood group O (50.3%). The discrepancy between our findings and previous studies might be related to different characteristics between general population and the blood donors. And our findings also reflected that individuals with blood group O might be more likely to make blood donation. The percentage of Rh (D) negative blood group in our study appeared as 1.02%, which was in accordance with the results (1.0%) of 26 199 apheresis platelet donations reported by Guo et al.[4], higher than the results (0.4%) of 512 594 whole blood donations reported by Guo et al.[4], while lower than findings (17.9%) in blood donations in Sweden and Denmark.[4]

Similar to findings from other countries, we found that frequencies of ABO and rhesus blood phenotypes differed in various ethnic groups. In our study, the O phenotype was about 41.81% in Zhuang population, while 27.91% in Uygur population. And Rh (D) negative phenotype were 3.33% in Uygur, while 0.34% in Mongolian and 0.36% in Manchu populations. Li et al.[18] also found that the proportions of Rh (D) negative phenotype were approximately 5% in Uygur donations but only 0.4% in Han donations. Garratty et al.[3] demonstrated that the percentages of group O were 39.8% in Asian donors, 56.5% in Hispanic donors and 54.6% in North American Indian donors in the United States. And they found that the proportions of Rh (D) negativity were 1.7% in Asian donors, 17.3% in White non-Hispanic donors and 9.7% in North American Indian donors in the United States.[3] Hamed et al.[5] showed that the percentages of Rh (D) negative phenotype were 3.55% in Black Africans and 6.49% in Moors among 10 116 volunteers who gave blood at the national blood transfusion center in Mauritania. The distributions of ethnic groups in our study were similar to the report of the Sixth National Population Census in China, with 91.6% in Han, 1.3% in Zhuang, 0.8% in Manchu, 0.7 in Miao and 0.4% in Mongolian.[19]

In this study, we found that the proportion of ORh- blood group was significant higher in Uygur (0.84%) than in other ethnic groups (0.08%-0.39%). The supply of the “universal” ORh- blood group on time and on demand to hospitals is an ongoing challenge.[20] In China, the whole blood

collection has increased rapidly since the past decade, from 6.75 million donations in 2006 to 12.32 million donations in 2011, however, still far from the ever-increasing demand.[9, 21] Hirani et al.[20] showed that, as patient blood management became more widespread, there was an international decline in the demand for red blood cell units with a 21% reduction between 2012 and 2015 in Australia.[20] On the contrary, the demand for the ORh- blood group was in fact proportionally increasing.[20, 22] Information on the distribution of the "universal" ORh- blood group in different ethnic groups is of improtance for making better rational strategies on blood collection and management in China, especially during the shortage of blood supply.

ABO and rhesus blood groups are hereditarily determined and have been previously found to be associated with diseases.[1, 2] Amundadottir et al.[23] conducted a two-stage genome-wide association study and identified an association between ABO blood group gene and pancreatic cancer. Zu et al. evaluated the relationship between ABO blood group and congenital heart disease in 39 042 consecutive inpatients in a 6-year cohort study and found that A blood group demonstrated a decreased risk for isolated congenital heart disease (odds ratio 0.82; 95% CI, 0.78-0.87). Zhou et al. [24] conducted a matched case-control study and found an association between both A blood group, HBV infection and the development of extrahepatic cholangiocarcinoma. Genetic trait might contribute to the link between ABO/Rh blood groups and disease susceptibility, and contribute to the diverse distribution of ABO/Rh blood groups in different ethnic groups as well.

To the best of our knowledge, this is the largest population-based study of ABO/Rh distribution in different ethnic groups among the general population in China. However, there were several limitations in our study. First, information on subtypes of ABO blood groups (e.g. A1, A2, A3, Aw, Ax, Ael) was not available in the NFPHEP, thus distributions of those ABO subtypes in different ethnic groups could not be further assessed. Second, we did not analyze all the ethnic minorities in China as lack of relative information. Nevertheless, we analyzed the eight minorities with larger size of population in this study. Third, willingness and histories of blood donation were not investigated in the NFPHEP that we could not provide specific evidence on donor recruitment.

In conclusion, ABO and rhesus blood phenotypes varied across different ethnic groups in China. The proportions of O phenotype was higher in Zhuang (41.81%) than that in other ethnic groups. And the proportions of Rh (D) negative phenotype appeared higher in Uygur (3.33%) than in Mongolian (0.34%) or Manchu (0.36%) ethnic groups. Diversities on the distribution of ABO/Rh blood groups in different ethnic groups should be considered when making rational and evidence-based strategies on blood collection and management.

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Contributors: JL and SZ searched the literature, designed the study, analyzed the data, interpreted the results, and drafted the manuscript. QW, HS and YZ collected the data and revised the manuscript. ML conceived the study, designed the study, supervised the study, interpreted the results, and revised the manuscript. All authors have read and approved the final manuscript. ML is the study guarantors. ML has the right to grant on behalf of all authors and does grant on behalf of all authors.

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Table 1. Socio-demographic characteristics of study population

Characteristics	Number	Proportion (%)
Gender		
Male	1 870 435	48.81
Female	1 961 599	51.19
Age (years)		
21-29	2 405 744	62.78
30-39	1 247 194	32.55
40-49	179 096	4.67
Ethnicity		
Han	3 473 527	90.64
Uygur	129 454	3.38
Zhuang	47 305	1.23
Manchu	33 182	0.87
Miao	27 637	0.72
Yi	19 659	0.51
Mongolian	18 996	0.50
Hui	11 471	0.30
Others	70 803	1.85
Region		
Eastern	857 763	22.38
Central	1 930 145	50.37
Western	1 044 126	27.25
Education		
Primary school or below	178 680	4.66
Junior high school	2 503 844	65.34
Senior high school	700 159	18.27
College or higher	449 351	11.73
Occupation		
Farmers	2 914 777	76.06
Workers	354 080	9.24
Others	563 177	14.70
Total	3 832 034	100.00

Table 2. Distribution of ABO blood groups in study population according to ethnicity

Ethnicity	Number	ABO phenotypes (%)			
		A*	B*	AB*	O*
Han	3 473 527	1 065 599 (30.68)	1 021 051 (29.40)	338 230 (9.74)	1 048 647 (30.19)
Uygur	129 454	39 745 (30.70)	39 857 (30.79)	13 727 (10.60)	36 125 (27.91)
Zhuang	47 305	11 917 (25.19)	13 006 (27.49)	2602 (5.50)	19 780 (41.81)
Manchu	33 182	8438 (25.43)	11 180 (33.69)	3132 (9.44)	10 432 (31.44)
Miao	27 637	7847 (28.39)	7435 (26.90)	1932 (6.99)	10 423 (37.71)
Yi	19 659	6675 (33.95)	5191 (26.41)	1778 (9.04)	6015 (30.60)
Mongolian	18 996	4983 (26.23)	6320 (33.27)	1840 (9.69)	5853 (30.81)
Hui	11 471	3411 (29.74)	3429 (29.89)	1134 (9.89)	3497 (30.49)
Others	70 803	21 550 (30.44)	19 963 (28.20)	5887 (8.31)	23 403 (33.05)
Total	3 832 034	1 170 165 (30.54)	1 127 432 (29.42)	370 262 (9.66)	1 164 175 (30.38)

*P<0.001.

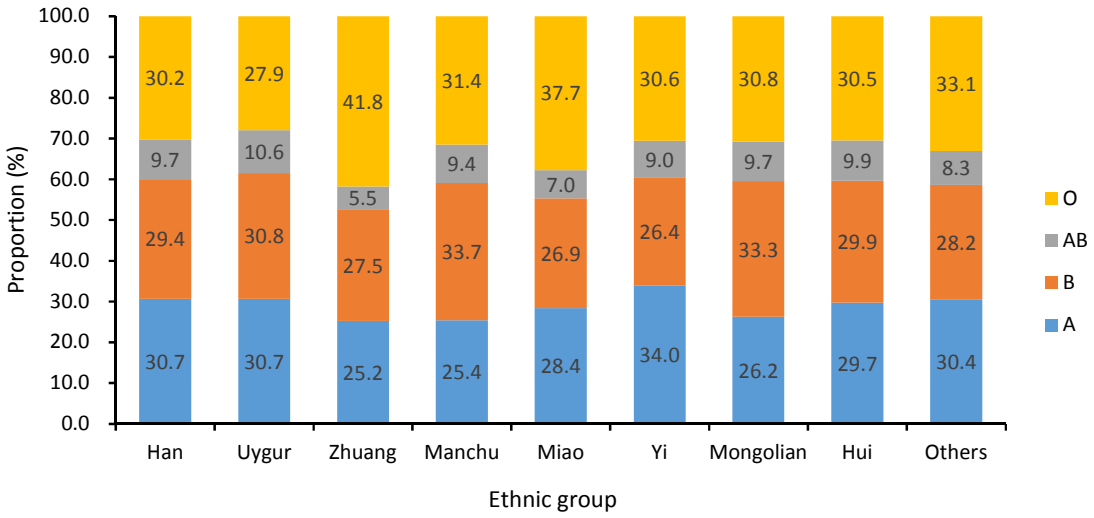

Figure 1. Distribution of ABO blood groups in different ethnic groups

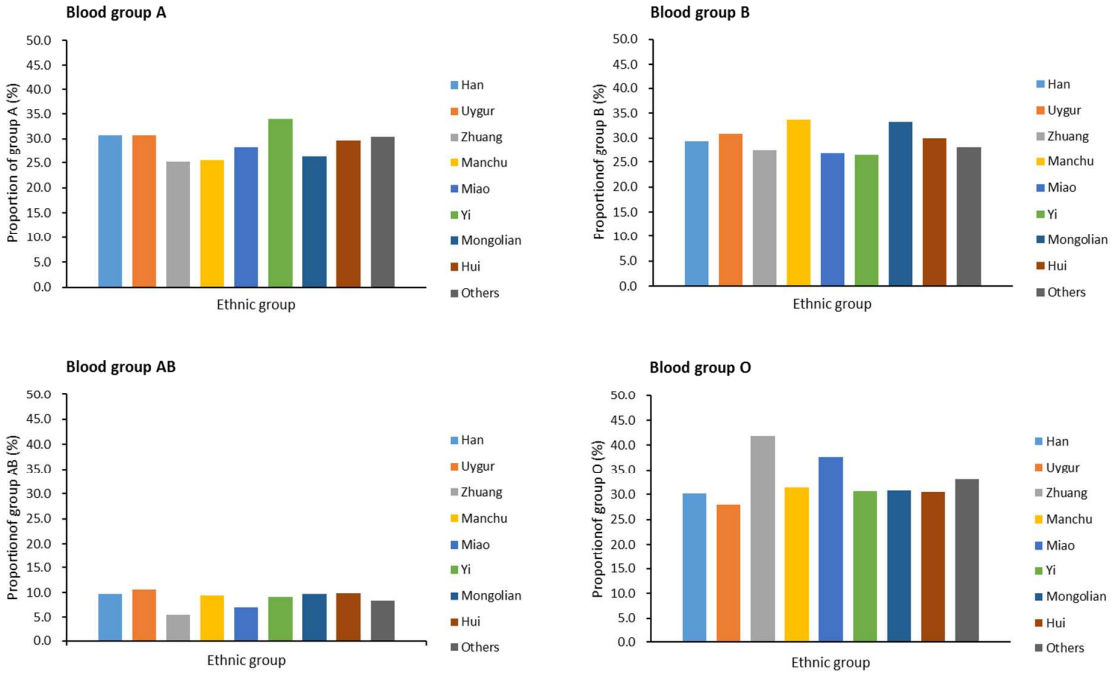

Figure 2. Proportion of ABO blood groups in different ethnic groups

Table 3. Distribution of rhesus blood groups in study population according to ethnicity

Ethnicity	Number	Rh (D) phenotypes (%)*	
		Positive	Negative
Han	3 473 527	3 440 524 (99.05)	33 003 (0.95)
Uygur	129 454	125 145 (96.67)	4309 (3.33)
Zhuang	47 305	47 065 (99.49)	240 (0.51)
Manchu	33 182	33 061 (99.64)	121 (0.36)
Miao	27 637	27 446 (99.31)	191 (0.69)
Yi	19 659	19 414 (98.75)	245 (1.25)
Mongolian	18 996	18 931 (99.66)	65 (0.34)
Hui	11 471	11 379 (99.20)	92 (0.80)
Others	70 803	70 064 (98.96)	739 (1.04)
Total	3 832 034	3 793 029 (98.98)	39 005 (1.02)

*P<0.001

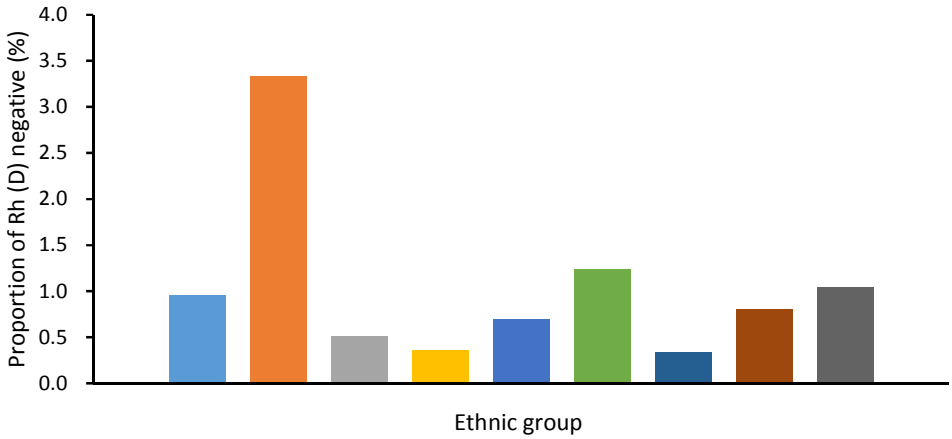

Figure 3. Proportion of Rh (D) positive blood group in different ethnic groups

Table 4. Distribution of ABO/Rh blood groups in study population according to ethnicity

Ethnicity	Number	Phenotypes (%)							
		ARh+	ARh-	BRh+	BRh-	ABRh+	ABRh-	ORh+	ORh-
Han	3 473 527	1 053 849 (30.34)	11 750 (0.34)	1 011 421 (29.12)	9630 (0.28)	335 237 (9.65)	2993 (0.09)	1 040 017 (29.94)	8630 (0.25)
Uygur	129 454	38 265 (29.56)	1480 (1.14)	38 529 (29.76)	1328 (1.03)	13 307 (10.28)	420 (0.32)	35 044 (27.07)	1081 (0.84)
Zhuang	47 305	11 821 (24.99)	96 (0.20)	12 938 (27.35)	68 (0.14)	2594 (5.48)	8 (0.02)	19 712 (41.67)	68 (0.14)
Manchu	33 182	8396 (25.30)	42 (0.13)	11 138 (33.57)	42 (0.13)	3123 (9.41)	9 (0.03)	10 404 (31.35)	28 (0.08)
Miao	27 637	7786 (28.17)	61 (0.22)	7372 (26.67)	63 (0.23)	1920 (6.95)	12 (0.04)	10 368 (37.51)	55 (0.20)
Yi	19 659	6601 (33.58)	74 (0.38)	5119 (26.04)	72 (0.37)	1755 (8.93)	23 (0.12)	5939 (30.21)	76 (0.39)
Mongolian	18 996	4968 (26.15)	15 (0.08)	6295 (33.14)	25 (0.13)	1834 (9.65)	6 (0.03)	5834 (30.71)	19 (0.10)
Hui	11 471	3381 (29.47)	30 (0.26)	3398 (29.62)	31 (0.27)	1124 (9.80)	10 (0.09)	3476 (30.30)	21 (0.18)
Others	70 803	21 320 (30.11)	230 (0.32)	19 731 (27.87)	232 (0.33)	5803 (8.20)	84 (0.12)	23 210 (32.78)	193 (0.27)
Total	3 832 034	1 156 387 (30.18)	13 778 (0.36)	1 115 941 (29.12)	11 491 (0.30)	366 697 (9.57)	3565 (0.09)	1 154 004 (30.11)	10 171 (0.27)

+, represented Rh (D) positive; -, represented Rh (D) negative.

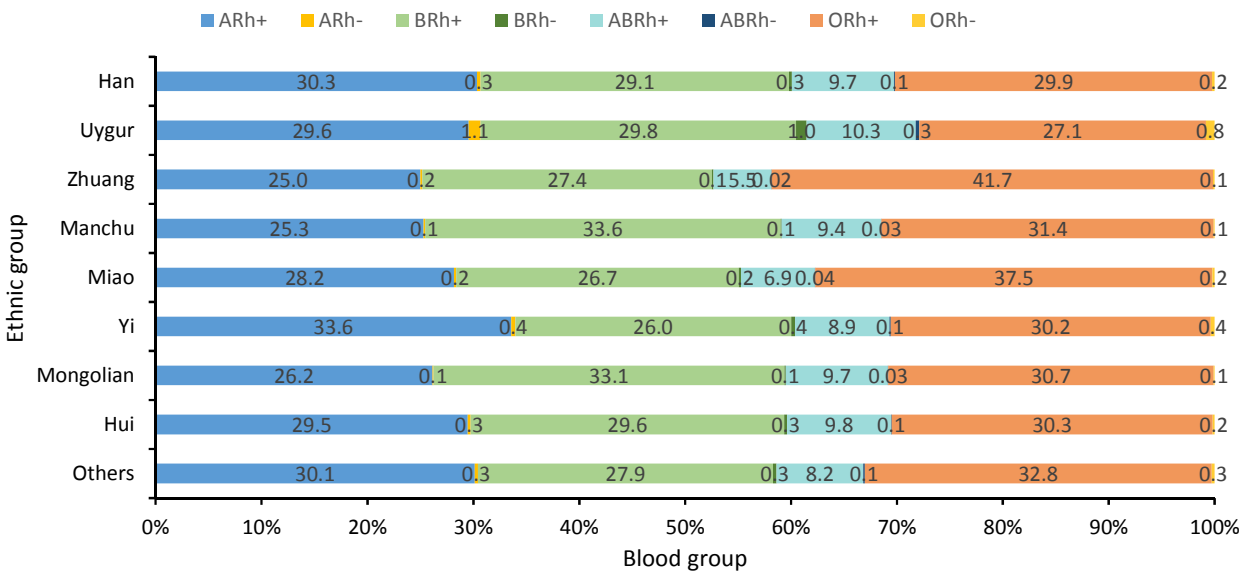

Figure 4. Distribution of ABO/Rh blood groups in different ethnic groups

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cross-sectional studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3
Objectives	3	State specific objectives, including any prespecified hypotheses	3
Methods			
Study design	4	Present key elements of study design early in the paper	3
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	3
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	3
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	4
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	3-4
Bias	9	Describe any efforts to address potential sources of bias	*4*
Study size	10	Explain how the study size was arrived at	3
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	4
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	4
		(*b*) Describe any methods used to examine subgroups and interactions	4
		(*c*) Explain how missing data were addressed	4
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	4
		(*e*) Describe any sensitivity analyses	Not applicable
Results			

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	4
		(b) Give reasons for non-participation at each stage	Not applicable
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	4
		(b) Indicate number of participants with missing data for each variable of interest	4
Outcome data	15*	Report numbers of outcome events or summary measures	4
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	4
		(*b*) Report category boundaries when continuous variables were categorized	4
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	Not applicable
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	5
Discussion			
Key results	18	Summarise key results with reference to study objectives	5-6
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	6
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	5-6
Generalisability	21	Discuss the generalisability (external validity) of the study results	6
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	7

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Title page

Title: Frequencies and ethnic distribution of ABO and rhesus D blood groups in China: a population-based cross-sectional study

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Abbreviations: RhD, rhesus D; RhD–, RhD negative; RhD+, RhD positive; NFPHEP, National Free Preconception Health Examination Project; CI, confidence interval.

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Frequencies and ethnic distribution of ABO and rhesus D blood groups in China: a population-based cross-sectional study

Abstract

Objectives ABO and rhesus D (RhD) blood groups are key factors affecting blood transfusion safety and clinical practice. The distribution of ABO and RhD blood groups varies globally. The distribution of ABO and RhD blood groups varies globally, but limited data exist for frequencies and ethnic distributions of ABO and RhD blood groups in Asian populations.

Design A population-based cross-sectional study.

Setting Data were obtained from the National Free Preconception Health Examination Project (NFPHEP) with participants from 220 counties of 31 provinces in China

Participants There were 3 832 034 participants aged 21 to 49 years who took part in the NFPHEP from January 2010 and December 2012 and were included, after excluding the participants without ABO and RhD blood types.

Outcome Measures The proportion of ABO and RhD blood groups among different ethnic groups was calculated.

Results ABO and RhD blood distribution was significantly different among nine ethnic groups (P<0.001). Compared with other ethnic groups, the Yi group had more A phenotypes (34.0%), and the Manchu (33.7%) and Mongolian (33.3%) ethnic groups had more B phenotypes. The Zhuang group had the greatest proportion of O phenotypes (41.8%), followed by the Miao group (37.7%). AB phenotypes were more frequent in the Uygur ethnic group (10.6%) but lower in the Zhuang group (5.5%). Meanwhile, RhD negativity (RhD–) was greater in the Uygur group (3.3%) than in the Mongolian (0.3%) and Manchu ethnic groups (0.4%). O RhD– blood groups were more frequent in the Uygur group (0.8%) than in the other ethnic groups (0.1%–0.4%, P<0.001).

Conclusion ABO and RhD blood phenotypes vary across different ethnic groups in China. The diversity in the distribution of the ABO and RhD blood groups in different ethnic groups should be considered when developing rational and evidence-based strategies for blood collection and management.

Strengths and limitations of this study

- To our knowledge, this is the largest population-based study of ABO and RhD blood type distribution in different ethnic groups among the general population in an Asian country.
- A major limitation of the study was that there was no further laboratory data on the subtypes of the ABO blood groups (e.g. A1, A2, A3, Aw, Ax, and Ael).
- We did not assess all of the 55 ethnic minority groups in China, but we assessed the 7 ethnic minority groups with larger population sizes.
- Participants' willingness to donate and history of blood donation were not investigated, so we could not provide specific evidence on donor recruitment.

Introduction

ABO and rhesus D (RhD) blood groups, the most well-known blood group systems, are of key importance for transfusion safety and clinical practice and are also thought to be linked with disease susceptibility [1, 2]. The distribution of ABO and RhD blood groups varies throughout the world;[3-5] previous studies have found the percentage of blood group O to be 46.6% in the United States[3], 34% in China[4], 49.10% in Mauritania[5], 38.9% in Sweden[6], and 42.3% in Denmark[6]. The proportion of those with RhD-negative (RhD–) blood has been reported to be 14.6% in the United States[3], 17.9% in Sweden and Denmark[6], and between 0.4%-1.0% in China[4]; this also varies among different races or ethnic populations.[3, 5, 7] In the United States, the percentage of group O varies from 39.8% in Asian donors to 56.5% in Hispanic donors, and the proportion of RhD– varies from 1.7% in Asian donors to 17.3% in White non-Hispanic donors.[3] Data regarding the distribution of ABO and RhD blood groups were primarily obtained from blood donors in previous studies, while little data came from the general population.

China composes more than 20% of the world's population, so its blood supply may potentially affect the global community.[8] Social–economic development and increased health care coverage have increased the demand for blood and its products in China[9]. Despite steady increases in total blood collections and voluntary non-remunerated donors, China faces challenges to its blood donation system.[10] 9% of Chinese donate blood, and more than 60% of donors are first-time donors.[10] Thus, data regarding the frequencies and ethnic distributions of ABO and RhD blood groups in the general population may help us to develop rational and evidence-based strategies for blood collection and management. However, studies that focused on the frequency and ethnic distribution of ABO and RhD blood groups in the general population have been scarce in China.

Thus, we conducted a large population-based study to investigate the distribution of ABO and RhD blood groups in different ethnic groups in the general population in China to provide reliable data for better development of rational strategies for blood collection and management.

Materials and methods

Study design and data source

We performed a nationwide population-based, cross-sectional study using data from the National Free Preconception Health Examination Project (NFPHEP), which is a national health check-up program that offers free preconception health examinations and counseling services for married couples preparing for pregnancy. It was launched by the Chinese National Health and Family Planning Commission and the Ministry of Finance in 2010. Project-related design and implementation were previously described[11-14]. This study was approved by the Institutional Review Board of the Chinese Association of Maternal and Child Health Studies. All participants were provided with written informed consent forms before enrollment.

From January 1, 2010, to December 31, 2012, there were 4 150 214 participants (2 120 131 women and 2 030 083 men) aged 21–49 years from 220 counties in 31 provinces enrolled in the NFPHEP, covering 86.1% of the target population[15]. 318 180 (7.7%) participants who did not undergo ABO and RhD blood typing were excluded, yielding 3 832 034 enrolled participants who were included for analysis.

Questionnaire and laboratory testing

Basic information was collected by trained local health workers from all of the participants in the

NFPHEP using a standardized questionnaire that inquired about gender, age, educational level, occupation, address of residence, and ethnicity (Han, Uygur, Zhuang, Manchu, Miao, Yi, Mongolian, Hui, or Others). During the physical examination, trained local health workers collected blood samples from all of the participants and immediately sent them to local laboratories. Testing for both the ABO and RhD blood groupings was performed simultaneously with reagents (anti-A, anti-B, anti-AB, and anti-D). The red blood cell agglutination method was used for blood type analysis. The National Center of Clinical Laboratories for Quality Inspection and Detection performed a biannual external quality assessment for quality control.

Statistical analysis

We used proportions to describe distributions of gender, age, ethnicity and other socio-demographic characteristics of the participants. We used Chi-square tests to compare proportions of A, B, AB and O blood groups across ethnicities. The proportion of RhD– and its 95% confidence interval (CI) was calculated. The Chi-square test was also used to compare the proportion of RhD– blood groups across ethnicities. Logistic regression was used to compare proportions of RhD– in the 8 ethnicities to that in the Han ethnicity. Odds ratio and its 95% CI was calculated in the logistic regression. According to the ABO phenotypes (A, B, AB, and O) and RhD phenotypes (RhD– and RhD+), we divided the participants into 8 blood groups, namely A RhD+, A RhD–, B RhD+, B RhD–, AB RhD+, AB RhD–, O RhD+ and O RhD–. We used the Chi-square test to compare distributions of ABO/RhD phenotypes across ethnicities. All of the analyses were done with SPSS version 18.0 (SPSS Inc., Chicago, IL, USA). Two-sided $p < 0.05$ was considered to be statistically significant.

Results

Socio-demographic characteristics of the study population

Of the 3 832 034 participants included in the study, 48.8% were male, 36.3% were older than 30 years of age, and 22.4% were living in the eastern areas of China. There were 3 473 527 (90.6%) of the participants who were of the Han ethnicity. The proportions of the Uygur, Zhuang, Manchu, Miao, Yi, Mongolian and Hui ethnicities were 3.4%, 1.2%, 0.9%, 0.7%, 0.5%, 0.5% and 0.3%, respectively (Table 1).

Distribution of ABO blood groups according to ethnicity

In the ABO blood system, blood group A (30.5%) appeared to be the most common phenotype, followed by O (30.4%), B (29.4%), and AB (9.7%). The proportions of the A, B, O, and AB blood groups were significantly different among the 9 ethnic groups (all $P < 0.001$, Table 2). Compared with the other ethnic groups, the Yi ethnic group had a significantly higher proportion of the A phenotype (34.0%), while Manchu (33.7%) and Mongolian (33.3%) ethnic groups had a significantly higher proportion of the B phenotype (all $P < 0.001$). The Zhuang ethnic group had the highest proportion of the O phenotype (41.8%), followed by the Miao ethnic group (37.7%). The proportion of the AB phenotype was significantly higher in the Uygur ethnic group (10.6%) but lower in the Zhuang ethnic group (5.5%, all $P < 0.001$). The distribution of the ABO blood groups according to ethnicity is shown in Figure 1.

Distribution of RhD blood groups according to ethnicity

In the rhesus blood system, 1.02% (95% CI: 1.01-1.03) of the 3 832 034 participants were RhD– (Table 3). The proportion of the RhD– group was significantly different among the 9 ethnic groups ($\chi^2 = 7413.07$, $P<0.001$). Compared with other ethnic groups, the proportion of RhD– appeared to

be significantly higher in the Uygur ethnic group (3.3%), while much lower in the Mongolian (0.3%) and Manchu ethnic groups (0.4%). The proportion of RhD– in the Yi (1.25%), Han (0.95%), and other ethnic groups (1.04%) was significantly different from each other (all P < 0.01). Compared with the Han ethnic group, participants of Uygur ethnicity (OR=3.59; 95% CI, 3.48-3.71), Yi ethnicity (OR=1.32; 95% CI, 1.16-1.49), and others (OR=1.10; 95% CI, 1.02-1.18) all had a significantly higher proportion of RhD–. The proportion of RhD– according to ethnicity is shown in Figure 2.

Distribution of ABO and RhD **blood groups according to ethnicity**

Compared with other ethnic groups, the Yi group had more A RhD+ phenotypes (33.6%), and the Uygur group had more A RhD– phenotypes (1.1%, all P < 0.001). O RhD– blood groups were more frequent in the Uygur group (0.8%) than in the other ethnic groups (0.1%–0.4%, P < 0.001). O RhD+ blood groups were frequent in the Zhuang group (41.7%) than in other ethnic groups (27.1%-37.5%, P < 0.001). The proportions of AB RhD+ blood group (10.3%) and AB RhD– blood group (0.3%) were both higher in the Uygur than in other ethnic groups (all P < 0.001). The distribution of ABO and RhD combination phenotypes across ethnicities is shown in Table 4.

Discussion

Similar with other developing countries, China has made progress on blood safety and availability through persistent efforts in the past decades.[16] China has 452 blood banks and 32 blood centers nationwide, but still faces challenges in limited donors and shortage of blood products.[16] How ABO/RhD blood groups are distributed in the general population is of interest to improve blood services. In this population-based study involving 3.8 million adults in China, we found that the A phenotype was the most common, followed by the O, B and AB phenotypes. Zu and colleagues.[17] reported A, O, B, and AB phenotypes to be 31.9%, 31.0%, 28.1%, and 9.1%, respectively, in 19 247 patients without congenital heart disease from the Shanghai Children's Medical Center in China, and these data agreed with ours. Guo and colleagues.[4] found that O phenotypes were the most frequent (34.0%), followed by A (29.0%), B (27.2%), and AB (8.8%) among 512,594 whole-blood donations at 5 centers in China from 2008 to 2009. These data differ from ours. Different characteristics between general population and blood donors might contribute to the discrepancy. One possible reason was that the proportions of Han ethnicity were lower in blood donors (86.2%) than in the general population (>90%).[4] The other possible explanation is that those with O type blood may donate more due to being universal donors. And this needs to be further addressed in future studies. RhD– phenotypes were 1.0% of the population, and these data agreed with Guo's group, who reported that the RhD– type was 1% of 26,199 apheresis platelet donors but 0.4% of 512,594 whole-blood donors.[4] These numbers are lower than data (17.9%) from Sweden and Denmark.[6]

The ABO and RhD blood phenotypes vary widely across races/ethnicities and geographical boundaries.[3, 18] We found that the O phenotype was more frequent in the Zhuang group (41.8%), and both RhD– phenotype (3.3%) and O RhD– phenotype (0.8%) were more frequent in the Uygur group in the general population. Literature regarding ethnic diversity on blood distribution among general population are limited, most of them from blood donors. Li and colleagues.[19] found that the proportions of the RhD– phenotype was approximately 5% in Uygur donations but only 0.4% in Han donations, which were consistent with ours. In the United States, Garratty and colleagues.[3] demonstrated that percentages of group O were 39.8% in Asian donors, 56.5% in

Hispanic donors and 54.6% in North American Indian donors. And they found that the proportions of RhD– was much lower in Asian donors (1.7%) than that in White non-Hispanic donors (17.3%) and North American Indian donors (9.7%).[3] Hamed and colleagues.[5] showed that the percentages of RhD– phenotype were 3.6% in Black Africans and 6.5% in Moors among 10 116 volunteers who gave blood at the national blood transfusion center in Mauritania. These findings highlight that it is necessary to consider ethnic diversity when developing recruitment strategies.

The majority of the population in China are of Han ethnicity (91.6%) and the minority of the population are of the other 55 ethnicities (8.4%), according to the Sixth National Population Census Report.[20] The Distribution of ethnic groups in our study was similar to this report. The Zhuang, Manchu, Uygur, Miao, Yi, Hui, and Mongolian populations were assessed in our study; they are the top seven ethnic groups among the 55 minorities. In China, whole blood collection has increased rapidly over the past decade, from 6.75 million donations in 2006 to 12.32 million donations in 2011; however, it is still far from the ever-increasing demand.[9, 21] Our findings on the ethnic diversity of blood group distribution would be helpful to design better recruitment strategies to prevent blood shortages.

Take group O RhD– for example, it is well-known that group O RhD– is a precious resource that are often in short supply.[22] Studies have shown that supplying the "universal" O RhD– blood group on time and on demand to hospitals is an ongoing challenge.[22-24] Hirani and colleagues.[23] showed that, as patient blood management became more widespread, there was an international decline in the demand for red blood cell units with a 21% reduction between 2012 and 2015 in Australia.[23] On the contrary, the demand for the O RhD– blood group was in fact proportionally increasing. [23,24] A significant proportion of O RhD– blood units were transfused to compatible, nonidentical recipients, although the frequency of this practice varied across sites from 0% to 33% in Australia.[22] The transfusion of group O RhD– blood to non-O RhD+ recipients can result in shortages of group O RhD– blood. Information on the distribution of the "universal" O RhD– blood group in different ethnic groups is of importance for developing better rational strategies for blood collection and management in China, especially during blood shortages. The proportion of group O RhD– was only 0.3% in the general population found in our study, thus it might be harder to encounter group O RhD– in Asian donors compared with Caucasian donors. However, the need for this precious resource still exists for O RhD– recipients, especially for trauma, obstetric and neonatal patients. The findings of a much higher proportion of group O RhD– in the Uygur population compared with other populations suggest that the government should make an extra effort to encourage people of the Uygur ethnicity to donate blood, especially for emergency blood supplies.

Besides of blood collection and management, from a preventive point of view on disease, understanding the distribution of blood groups can also provide information on the potential risk of diseases for the general population. ABO and RhD blood groups are reported to be associated with many diseases.[1, 2] Zu and colleagues.[17] evaluated the relationship between the ABO blood group and congenital heart disease in 39 042 consecutive inpatients in a 6-year cohort study and found that the A blood group demonstrated a decreased risk for isolated congenital heart disease (odds ratio 0.82; 95% CI, 0.78-0.87). Amundadottir and colleagues.[25] conducted a two-stage genome-wide association study and identified an association between the ABO blood group gene and pancreatic cancer. Genetic traits might contribute to the link between ABO and RhD blood

groups and disease susceptibility, and contribute to the diverse distribution of ABO and RhD blood groups in different ethnic groups as well.

To our knowledge, this is the largest population-based study of ABO and RhD blood type distributions across ethnicities in China. However, there were several limitations in our study. First, information on the subtypes of the ABO blood groups (e.g. A1, A2, A3, Aw, Ax, and Ael) was not available in the NFPHEP, thus the distribution of those ABO subtypes could not further be assessed. Second, we did not assess all of the 55 ethnic minorities in China. Nevertheless, we assessed 7 minorities with a large-sized population. Third, donor willingness and histories of blood donation were not investigated in the NFPHEP, so we could not provide specific evidence on donor recruitment.

In conclusion, ABO and RhD blood phenotypes varied across ethnicities in China. Diversity in the distribution of the ABO and RhD blood groups in different ethnic groups should be considered when developing rational and evidence-based strategies for blood collection and management. Our data should allow targeted donor management to increase the proportion of needed blood type products, especially for blood types that are high in demand but low in supply.

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Contributors: JL and SZ searched the literature, designed the study, analyzed the data, interpreted the results, and drafted the manuscript. QW, HS and YZ collected the data and revised the manuscript. ML conceived the study, designed the study, supervised the study, interpreted the results, and revised the manuscript. All authors have read and approved the final manuscript. ML is the study guarantors. ML has the right to grant on behalf of all authors and does grant on behalf of all authors.

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Provenance and peer review Not commissioned; externally peer reviewed.

Data sharing statement: Due to privacy and ethical concerns, supporting data cannot be made openly available. Please contact the authors for the access of the original data.

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Table 1. Socio-demographic characteristics of the study population

Characteristic	Total (%)	Male (%)	Female (%)
Ethnicity			
Han	3473527 (90.6)	1698090 (90.8)	1775437 (90.5)
Uygur	129454 (3.4)	64559 (3.5)	64895 (3.3)
Zhuang	47305 (1.2)	22735 (1.2)	24570 (1.3)
Manchu	33182 (0.9)	16988 (0.9)	16194 (0.8)
Miao	27637 (0.7)	12212 (0.7)	15425 (0.8)
Yi	19659 (0.5)	8839 (0.5)	10820 (0.6)
Mongolian	18996 (0.5)	9148 (0.5)	9848 (0.5)
Hui	11471 (0.3)	5588 (0.3)	5883 (0.3)
Others	70803 (1.8)	32276 (1.7)	38527 (2.0)
Age (years)			
21-29	2405744 (62.8)	1035243 (55.3)	1370501 (69.9)
30-39	1247194 (32.5)	723523 (38.7)	523671 (26.7)
40-49	179096 (4.7)	111669 (6.0)	67427 (3.4)
Region			
Eastern	857763 (22.4)	416191 (22.3)	441572 (22.5)
Central	1930145 (50.4)	945877 (50.6)	984268 (50.2)
Western	1044126 (27.2)	508367 (27.2)	535759 (27.3)
Education			
Primary school or below	178680 (4.7)	80321 (4.3)	98359 (5.0)
Junior high school	2503844 (65.3)	1202193 (64.3)	1301651 (66.4)
Senior high school	700159 (18.3)	358423 (19.2)	341736 (17.4)
College or higher	449351 (11.7)	229498 (12.3)	219853 (11.2)
Occupation			
Farmers	2914777 (76.1)	1403135 (75.0)	1511642 (77.1)
Workers	354080 (9.2)	197556 (10.6)	156524 (8.0)
Others	563177 (14.7)	269744 (14.4)	293433 (15.0)
Total	3832034 (100.0)	1870435 (100.0)	1961599 (100.0)

Table 2. Distribution of ABO blood groups in the study population according to ethnicity

Ethnicity	Number	ABO phenotype (%)			
		A	B	AB	O
Han	3 473 527	1 065 599 (30.7)	1 021 051 (29.4)	338 230 (9.7)	1 048 647 (30.2)
Uygur	129 454	39 745 (30.7)	39 857 (30.8)	13 727 (10.6)*	36 125 (27.9)
Zhuang	47 305	11 917 (25.2)	13 006 (27.5)	2602 (5.5)	19 780 (41.8)*
Manchu	33 182	8438 (25.4)	11 180 (33.7)*	3132 (9.4)	10 432 (31.4)
Miao	27 637	7847 (28.4)	7435 (26.9)	1932 (7.0)	10 423 (37.7)*
Yi	19 659	6675 (34.0)*	5191 (26.4)	1778 (9.0)	6015 (30.6)
Mongolian	18 996	4983 (26.2)	6320 (33.3)*	1840 (9.7)	5853 (30.8)
Hui	11 471	3411 (29.7)	3429 (29.9)	1134 (9.9)	3497 (30.5)
Others	70 803	21 550 (30.4)	19 963 (28.2)	5887 (8.3)	23 403 (33.1)
Total	3 832 034	1 170 165 (30.5)	1 127 432 (29.4)	370 262 (9.7)	1 164 175 (30.4)

* Compared with the other ethnic groups, the proportions of group A (B, AB, or O) were all significantly higher (P<0.001).

Table 3. Distribution of RhD blood groups in the study population according to ethnicity

Ethnicity	Total	RhD–		Odds Ratio (95% CI)
		N	Proportion (%, 95% CI)	
Han	3 473 527	33 003	0.95 (0.94-0.96)	1 (Reference)
Uygur	129 454	4309	3.33 (3.23-3.43)[a]	3.59 (3.48-3.71)*
Zhuang	47 305	240	0.51 (0.44-0.57)	0.53 (0.47-0.60)*
Manchu	33 182	121	0.36 (0.30-0.43)	0.38 (0.32-0.46)*
Miao	27 637	191	0.69 (0.59-0.79)	0.73 (0.63-0.84)*
Yi	19 659	245	1.25 (1.09-1.40)	1.32 (1.16-1.49)*
Mongolian	18 996	65	0.34 (0.26-0.43)	0.36 (0.28-0.46)*
Hui	11 471	92	0.80 (0.64-0.97)	0.84 (0.69-1.04)
Others	70 803	739	1.04 (0.97-1.12)	1.10 (1.02-1.18)*
Total	3 832 034	39 005	1.02 (1.01-1.03)	

RhD–, RhD negative; CI, confidence interval; *, P<0.001.

[a] Compared with the other ethnic groups, the proportions of the RhD– group was significantly higher in the Uygur population (all P<0.001).

Table 4. Distribution of ABO and RhD blood groups in the study population according to ethnicity

Ethnicity	Number	Phenotype (%)							
		A RhD+	A RhD–	B RhD+	B RhD–	AB RhD+	AB RhD–	O RhD+	O RhD–
Han	3 473 527	1 053 849 (30.3)	11 750 (0.3)	1 011 421 (29.1)	9630 (0.3)	335 237 (9.7)	2993 (0.1)	1 040 017 (29.9)	8630 (0.3)
Uygur	129 454	38 265 (29.6)	1480 (1.1)	38 529 (29.8)	1328 (1.0)	13 307 (10.3)	420 (0.3)	35 044 (27.1)	1081 (0.8)
Zhuang	47 305	11 821 (25.0)	96 (0.2)	12 938 (27.4)	68 (0.1)	2594 (5.5)	8 (0.02)	19 712 (41.7)	68 (0.1)
Manchu	33 182	8396 (25.3)	42 (0.1)	11 138 (33.6)	42 (0.1)	3123 (9.4)	9 (0.03)	10 404 (31.6)	28 (0.1)
Miao	27 637	7786 (28.2)	61 (0.2)	7372 (26.7)	63 (0.2)	1920 (7.0)	12 (0.04)	10 368 (37.5)	55 (0.2)
Yi	19 659	6601 (33.6)	74 (0.4)	5119 (26.0)	72 (0.4)	1755 (8.9)	23 (0.1)	5939 (30.2)	76 (0.4)
Mongolian	18 996	4968 (26.2)	15 (0.1)	6295 (33.1)	25 (0.1)	1834 (9.7)	6 (0.03)	5834 (30.7)	19 (0.1)
Hui	11 471	3381 (29.5)	30 (0.3)	3398 (29.6)	31 (0.3)	1124 (9.8)	10 (0.1)	3476 (30.3)	21 (0.2)
Others	70 803	21 320 (30.1)	230 (0.3)	19 731 (27.9)	232 (0.3)	5803 (8.2)	84 (0.1)	23 210 (32.8)	193 (0.3)
Total	3 832 034	1 156 387 (30.2)	13 778 (0.4)	1 115 941 (29.1)	11 491 (0.3)	366 697 (9.6)	3565 (0.1)	1 154 004 (30.1)	10 171 (0.3)

RhD+ represents RhD positive, and RhD– represents RhD–.

Figure 1. Distribution of ABO blood groups in different ethnic groups

Figure 2. Proportion of the RhD- blood group in different ethnic groups

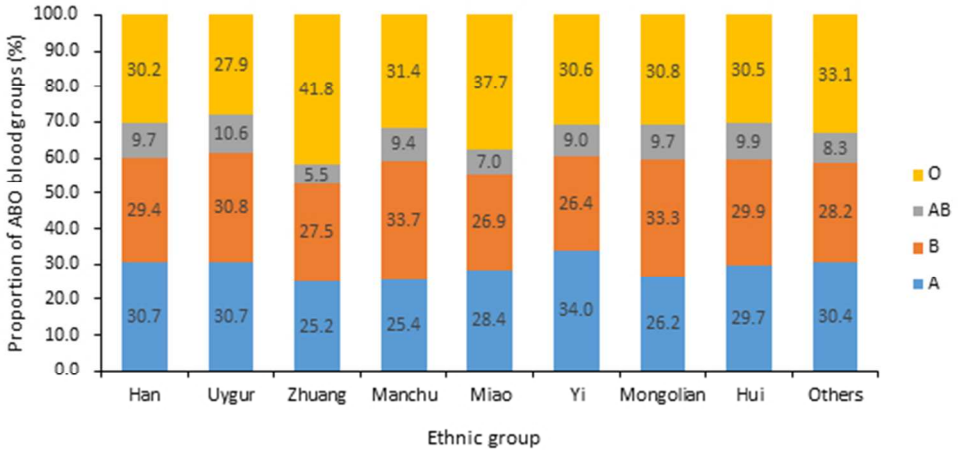

Figure 1. Distribution of ABO blood groups in different ethnic groups

51x24mm (300 x 300 DPI)

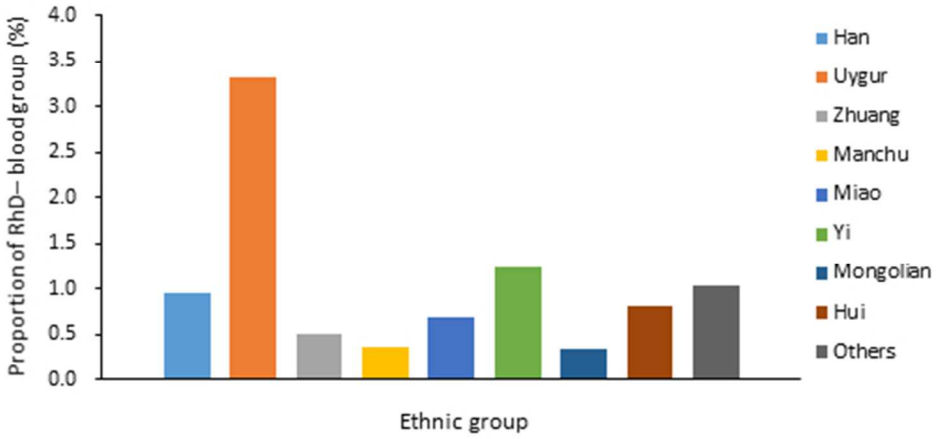

Figure 2. Proportion of the RhD- blood group in different ethnic groups

45x22mm (300 x 300 DPI)

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cross-sectional studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3
Objectives	3	State specific objectives, including any prespecified hypotheses	3
Methods			
Study design	4	Present key elements of study design early in the paper	3
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	3
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	3
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	4
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	3-4
Bias	9	Describe any efforts to address potential sources of bias	*4*
Study size	10	Explain how the study size was arrived at	3
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	4
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	4
		(*b*) Describe any methods used to examine subgroups and interactions	4
		(*c*) Explain how missing data were addressed	4
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	4
		(*e*) Describe any sensitivity analyses	Not applicable
Results			

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	4
		(b) Give reasons for non-participation at each stage	Not applicable
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	4
		(b) Indicate number of participants with missing data for each variable of interest	4
Outcome data	15*	Report numbers of outcome events or summary measures	4
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	4
		(*b*) Report category boundaries when continuous variables were categorized	4
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	Not applicable
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	5
Discussion			
Key results	18	Summarise key results with reference to study objectives	5-6
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	6
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	5-6
Generalisability	21	Discuss the generalisability (external validity) of the study results	6
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	7

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Frequencies and ethnic distribution of ABO and RhD blood groups in China: a population-based cross-sectional study

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Title page

Title: Frequencies and ethnic distribution of ABO and RhD blood groups in China: a population-based cross-sectional study

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Abbreviations: RhD–, RhD negative; RhD+, RhD positive; NFPHEP, National Free Preconception Health Examination Project; CI, confidence interval.

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Frequencies and ethnic distribution of ABO and RhD blood groups in China: a population-based cross-sectional study

Abstract

Objectives ABO and RhD blood groups are key factors affecting blood transfusion safety. The distribution of ABO and RhD blood groups varies globally, but limited data exist for ethnic distributions of these blood groups in Asian populations. We aimed to evaluate the distribution of ABO and RhD blood groups among Chinese ethnic groups.

Design A population-based cross-sectional study.

Setting Data on ABO groups and ethnicities were obtained from the National Free Preconception Health Examination Project (NFPHEP) with participants from 220 counties of 31 provinces in China

Participants There were 3 832 034 participants aged 21 to 49 years who took part in the NFPHEP from January 2010 and December 2012 and were included, after excluding the participants without ABO and RhD blood types.

Outcome Measures The proportion of ABO and RhD blood groups among different ethnic groups was calculated.

Results ABO and RhD blood distribution was significantly different among nine ethnic groups (P<0.001). Compared with other ethnic groups, the Yi group had more A phenotypes (34.0%), and the Manchu (33.7%) and Mongolian (33.3%) ethnic groups had more B phenotypes. The Zhuang group had the greatest proportion of O phenotypes (41.8%), followed by the Miao group (37.7%). AB phenotypes were more frequent in the Uygur ethnic group (10.6%) but lower in the Zhuang group (5.5%). Meanwhile, RhD negativity (RhD–) was greater in the Uygur group (3.3%) than in the Mongolian (0.3%) and Manchu ethnic groups (0.4%). O RhD– blood groups were more frequent in the Uygur group (0.8%) than in the other ethnic groups (0.1%–0.4%, P<0.001).

Conclusion ABO and RhD blood phenotypes vary across different ethnic groups in China. The diversity in the distribution of the ABO and RhD blood groups in different ethnic groups should be considered when developing rational and evidence-based strategies for blood collection and management.

Strengths and limitations of this study

- To our knowledge, this is the largest population-based study of ABO and RhD blood type distribution in different ethnic groups among the general population in an Asian country.
- A major limitation of the study was that there was no further laboratory data on the subtypes of the ABO blood groups (e.g. A1, A2, A3, Aw, Ax, and Ael).
- We did not assess all of the 55 ethnic minority groups in China, but we assessed the 7 ethnic minority groups with larger population sizes.
- Participants' willingness to donate and history of blood donation were not investigated, so we could not provide specific evidence on donor recruitment.

Introduction

ABO and RhD blood groups, the most well-known blood group systems, are of key importance for transfusion safety and clinical practice and are also thought to be linked with disease susceptibility [1, 2]. The distribution of ABO and RhD blood groups varies throughout the world;[3-5] previous studies have found the percentage of blood group O to be 46.6% in the United States[3], 34% in China[4], 49.10% in Mauritania[5], 38.9% in Sweden[6], and 42.3% in Denmark[6]. The proportion of those with RhD-negative (RhD–) blood has been reported to be 14.6% in the United States[3], 17.9% in Sweden and Denmark[6], and between 0.4%-1.0% in China[4]; this also varies among different races or ethnic populations.[3, 5, 7] In the United States, the percentage of group O varies from 39.8% in Asian donors to 56.5% in Hispanic donors, and the proportion of RhD– varies from 1.7% in Asian donors to 17.3% in White non-Hispanic donors.[3] Data regarding the distribution of ABO and RhD blood groups were primarily obtained from blood donors in previous studies, whilst little data came from the general population.

China comprises more than 20% of the world's population.[8] Social–economic development and increased health care coverage have increased the demand for blood and its products in China[9]. Despite steady increases in total blood collections and voluntary non-remunerated donors, China faces challenges to its blood donation system.[10] 9% of Chinese donate blood, and more than 60% of donors are first-time donors.[10] Thus, data regarding the frequencies and ethnic distributions of ABO and RhD blood groups in the general population may help us to develop rational and evidence-based strategies for blood collection and management. However, studies that focused on the frequency and ethnic distribution of ABO and RhD blood groups in the general population have been scarce in China.

Thus, we conducted a large population-based study to investigate the distribution of ABO and RhD blood groups in different ethnic groups in the general population in China to provide reliable data for better development of rational strategies for blood collection and management.

Materials and methods

Study design and data source

We performed a nationwide population-based, cross-sectional study using data from the National Free Preconception Health Examination Project (NFPHEP), which is a national health check-up program that offers free preconception health examinations and counseling services for married couples preparing for pregnancy. It was launched by the Chinese National Health and Family Planning Commission and the Ministry of Finance in 2010. Project-related design and implementation were previously described[11-14]. This study was approved by the Institutional Review Board of the Chinese Association of Maternal and Child Health Studies. All participants were provided with written informed consent forms before enrollment.

From January 1, 2010, to December 31, 2012, there were 4 150 214 participants (2 120 131 women and 2 030 083 men) aged 21–49 years from 220 counties in 31 provinces enrolled in the NFPHEP, covering 86.1% of the target population[15]. 318 180 (7.7%) participants who did not undergo ABO and RhD blood typing were excluded, yielding 3 832 034 enrolled participants who were included for analysis.

Questionnaire and laboratory testing

Basic information was collected by trained local health workers from all of the participants in the

NFPHEP using a standardized questionnaire that inquired about gender, age, educational level, occupation, address of residence, and ethnicity (Han, Uygur, Zhuang, Manchu, Miao, Yi, Mongolian, Hui, or Others). During the physical examination, trained local health workers collected blood samples from all of the participants and immediately sent them to local laboratories. Testing for both the ABO and RhD blood groupings was performed simultaneously with reagents (anti-A, anti-B, anti-AB, and anti-D). The red blood cell agglutination method was used for blood type analysis. The National Center of Clinical Laboratories for Quality Inspection and Detection performed a biannual external quality assessment for quality control.

Statistical analysis

We used proportions to describe distributions of gender, age, ethnicity and other socio-demographic characteristics of the participants. We used Chi-square tests to compare proportions of A, B, AB and O blood groups across ethnicities. The proportion of RhD– and its 95% confidence interval (CI) was calculated. The Chi-square test was also used to compare the proportion of RhD– blood groups across ethnicities. According to the ABO phenotypes (A, B, AB, and O) and RhD phenotypes (RhD– and RhD+), we divided the participants into 8 blood groups, namely A RhD+, A RhD–, B RhD+, B RhD–, AB RhD+, AB RhD–, O RhD+ and O RhD–. We used the Chi-square test to compare distributions of ABO/RhD phenotypes across ethnicities. All of the analyses were done with SPSS version 18.0 (SPSS Inc., Chicago, IL, USA). Two-sided $p < 0.05$ was considered to be statistically significant.

Results

Demographic characteristics of the study population

Of the 3 832 034 participants included in the study, 48.8% were male, 36.3% were older than 30 years of age. There were 3 473 527 (90.6%) of the participants who were of the Han ethnicity. The proportions of the Uygur, Zhuang, Manchu, Miao, Yi, Mongolian and Hui ethnicities were 3.4%, 1.2%, 0.9%, 0.7%, 0.5%, 0.5% and 0.3%, respectively (Table 1). The Manchu ethnic group (51.2%) had a significantly higher proportion of male proportion than other ethnicities (all $P < 0.001$).

Distribution of ABO blood groups according to ethnicity

In the ABO blood system, blood group A (30.5%) appeared to be the most common phenotype, followed by O (30.4%), B (29.4%), and AB (9.7%). The proportions of the A, B, O, and AB blood groups were significantly different among the 9 ethnic groups (all $P < 0.001$, Table 2). Compared with the other ethnic groups, the Yi ethnic group had a significantly higher proportion of the A phenotype (34.0%), while Manchu (33.7%) and Mongolian (33.3%) ethnic groups had a significantly higher proportion of the B phenotype (all $P < 0.001$). The Zhuang ethnic group had the highest proportion of the O phenotype (41.8%), followed by the Miao ethnic group (37.7%). The proportion of the AB phenotype was significantly higher in the Uygur ethnic group (10.6%) but lower in the Zhuang ethnic group (5.5%, all $P < 0.001$).

Distribution of RhD blood groups according to ethnicity

In the Rh blood system, 1.02% (95% CI: 1.01-1.03) of the 3 832 034 participants were RhD– (Table 3). The proportion of the RhD– group was significantly different among the 9 ethnic groups ($\chi^2 = 7413.07$, $P<0.001$). Compared with other ethnic groups, the proportion of RhD– appeared to be significantly higher in the Uygur ethnic group (3.3%), while much lower in the Mongolian (0.3%) and Manchu ethnic groups (0.4%). The proportion of RhD– in the Yi (1.25%), Han (0.95%), and

other ethnic groups (1.04%) was significantly different from each other (all P < 0.01). Compared with the Han ethnic group, participants of Uygur ethnicity (OR=3.59; 95% CI, 3.48-3.71), Yi ethnicity (OR=1.32; 95% CI, 1.16-1.49), and others (OR=1.10; 95% CI, 1.02-1.18) all had a significantly higher proportion of RhD–.

Distribution of ABO and RhD blood groups according to ethnicity

Compared with other ethnic groups, the Yi group had more A RhD+ phenotypes (33.6%), and the Uygur group had more A RhD– phenotypes (1.1%, all P < 0.001). O RhD– blood groups were more frequent in the Uygur group (0.8%) than in the other ethnic groups (0.1%–0.4%, P < 0.001). O RhD+ blood groups were frequent in the Zhuang group (41.7%) than in other ethnic groups (27.1%-37.5%, P < 0.001). The proportions of AB RhD+ blood group (10.3%) and AB RhD– blood group (0.3%) were both higher in the Uygur than in other ethnic groups (all P < 0.001). The distribution of ABO and RhD combination phenotypes across ethnicities is shown in Table 4.

Discussion

Similar with other developing countries, China has made progress on blood safety and availability through persistent efforts on blood screening and supply in the past decades.[16] China has 452 blood banks and 32 blood centers nationwide, but still faces challenges in limited donors and blood shortage.[16] How ABO/RhD blood groups are distributed in the general population is of interest to improve blood services.

In this population-based study involving 3.8 million adults in China, we found that the A phenotype was the most common, followed by the O, B and AB phenotypes; O phenotype was more frequent in the Zhuang group (41.8%); and RhD– phenotype (3.3%) was more frequent in the Uygur group. Zu and colleagues[17] reported A, O, B, and AB phenotypes to be 31.9%, 31.0%, 28.1%, and 9.1%, respectively, in 19 247 patients without congenital heart disease in China, which were similar with our findings. This was a general population of patients with heart disease, therefore the data matches closely to our study conducted as there were likely to be all ethnicities present. In the Chinese blood donors, Guo and colleagues[4] reported that O phenotype was the most frequent (34.0%) and RhD– phenotype was 1.0% among 512,594 donations at 5 blood centers in China. Different characteristics between general population and blood donors might contribute to the discrepancy on ABO distribution, because it was found that Han donors were under-represented (86.2%) compared to the general population (>90%).[4] Li and colleagues[18] found that RhD- donors were more prevalent especially from the Uygur population (5%), which was consistent with the findings from the general population. However, these numbers are much lower than data (17.9% for RhD- phenotype) from Sweden and Denmark.[6] In the United States, Garratty and colleagues[3] demonstrated that percentages of group O were 39.8% in Asian donors, 56.5% in Hispanic donors and 54.6% in North American Indian donors. And they found that the proportions of RhD– was much lower in Asian donors (1.7%) than that in White non-Hispanic donors (17.3%) and North American Indian donors (9.7%).[3] The ABO and RhD blood phenotypes vary widely across races/ethnicities and geographical boundaries.[3, 19] These findings highlight that it is necessary to consider ethnic diversity when developing recruitment strategies.

The majority of the population in China are of Han ethnicity (91.6%) and the minority of the population are of the other 55 ethnicities (8.4%), according to the Sixth National Population Census Report.[20] The Distribution of ethnic groups in our study was similar to this report. The Zhuang, Manchu, Uygur, Miao, Yi, Hui, and Mongolian populations were assessed in our study;

they are the top seven ethnic groups among the 55 minorities. In China, whole blood collection has increased rapidly over the past decade, from 6.75 million donations in 2006 to 12.32 million donations in 2011; however, it is still far from the ever-increasing demand.[9, 21] Our findings on the ethnic diversity of blood group distribution would be helpful to design better recruitment strategies to prevent blood shortages.

Take group O RhD– for example, it is well-known that group O RhD– is a precious resource that are often in short supply.[22] Studies have shown that supplying the "universal" O RhD– blood group on time and on demand to hospitals is an ongoing challenge.[22-24] Hirani and colleagues.[23] showed that, as patient blood management became more widespread, there was an international decline in the demand for red blood cell units with a 21% reduction between 2012 and 2015 in Australia.[23] On the contrary, the demand for the O RhD– blood group was in fact proportionally increasing. [23,24] A significant proportion of O RhD– blood units were transfused to compatible, non-identical recipients, although the frequency of this practice varied across sites from 0% to 33% in Australia.[22] The transfusion of group O RhD– blood to non-O RhD+ recipients can result in shortages of group O RhD– blood. Interestingly, we found that 98.98% of the population was RhD+ and only 0.3% were O RhD– blood in the Chinese general population. Given the high proportion of RhD+, the likelihood of emergency/trauma patients being RhD- and therefore susceptible to alloimmunization are so remote that collections of O Rh(D)+ might be more sensible. Studies has showed that transfusing emergency patients with unknown blood type with O RhD+ red blood cell concentrates has a low risk of inducing anti-D antibodies (3%-7%).[25-26] RhD- blood types may not be as vitally required in China as in other countries with high proportion of RhD- blood. Information on the distribution of the O RhD+ and O RhD- blood groups in different ethnic groups is of importance for developing better rational strategies for blood collection and management in China, especially during blood shortages.

ABO and RhD blood groups are reported to be associated with many diseases.[1, 2] Understanding the distribution of blood groups in the general population can provide information on the potential risk of diseases based on their blood groups. Zu and colleagues.[17] evaluated the relationship between the ABO blood group and congenital heart disease in 39 042 consecutive inpatients in a 6-year cohort study and found that the A blood group demonstrated a decreased risk for isolated congenital heart disease (odds ratio 0.82; 95% CI, 0.78-0.87). Amundadottir and colleagues.[27] conducted a two-stage genome-wide association study and identified an association between the ABO blood group gene and pancreatic cancer. Genetic traits might contribute to the link between ABO and RhD blood groups and disease susceptibility, and contribute to the diverse distribution of ABO and RhD blood groups in different ethnic groups as well.

To our knowledge, this is the largest population-based study of ABO and RhD blood type distributions across ethnicities in China. However, there were several limitations in our study. First, information on the subtypes of the ABO blood groups (e.g. A1, A2, A3, Aw, Ax, and Ael) was not available in the NFPHEP, thus the distribution of those ABO subtypes could not further be assessed. Second, we did not assess all of the 55 ethnic minorities in China. Nevertheless, we assessed 7 minorities with a large-sized population. Third, donor willingness and histories of blood donation were not investigated in the NFPHEP, so we could not provide specific evidence on donor recruitment.

In conclusion, ABO and RhD blood phenotypes varied across ethnicities in China. Diversity in the distribution of the ABO and RhD blood groups in different ethnic groups should be considered

when developing rational and evidence-based strategies for blood collection and management. Our data should allow targeted donor management to increase the proportion of needed blood type products, especially for blood types that are high in demand but low in supply.

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Contributors: JL and SZ searched the literature, designed the study, analyzed the data, interpreted the results, and drafted the manuscript. QW, HS and YZ collected the data and revised the manuscript. ML conceived the study, designed the study, supervised the study, interpreted the results, and revised the manuscript. All authors have read and approved the final manuscript. ML is the study guarantors. ML has the right to grant on behalf of all authors and does grant on behalf of all authors.

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Table 1. Socio-demographic characteristics of the study population

Characteristic	Total (%)	Male (%)	Female (%)
Ethnicity			
Han	3473527 (90.6)	1 698 090 (48.9)	1 775 437 (51.1)
Uygur	129454 (3.4)	64 559 (49.9)	64 895 (50.1)
Zhuang	47305 (1.2)	22 735 (48.1)	24 570 (51.9)
Manchu	33182 (0.9)	16 988 (51.2)*	16 194 (48.8)
Miao	27637 (0.7)	12 212 (44.2)	15 425 (55.8)
Yi	19659 (0.5)	8839 (45.0)	10 820 (55.0)
Mongolian	18996 (0.5)	9148 (48.2)	9848 (51.8)
Hui	11471 (0.3)	5588 (48.7)	5883 (51.3)
Others	70803 (1.8)	32 276 (45.6)	38 527 (54.4)
Age (years)			
21-29	2 405 744 (62.8)	1 035 243 (43.0)	1 370 501 (57.0)
30-39	1 247 194 (32.5)	723 523 (58.0)	523 671 (42.0)
40-49	179 096 (4.7)	111 669 (62.4)	67 427 (37.6)
Region			
Eastern	857 763 (22.4)	416 191 (48.5)	441 572 (51.5)
Central	1 930 145 (50.4)	945 877 (49.0)	984 268 (51.0)
Western	1 044 126 (27.2)	508 367 (48.7)	535 759 (51.3)
Education			
Primary school or below	178 680 (4.7)	80 321 (45.0)	98 359 (55.0)
Junior high school	2 503 844 (65.3)	1 202 193 (48.0)	1 301 651 (52.0)
Senior high school	700 159 (18.3)	358 423 (51.2)	341 736 (48.8)
College or higher	449 351 (11.7)	229 498 (51.1)	219 853 (48.9)
Occupation			
Farmers	2 914 777 (76.1)	1 403 135 (48.1)	1 511 642 (51.9)
Factory workers	354 080 (9.2)	197 556 (55.8)	156 524 (44.2)
Others	563 177 (14.7)	269 744 (47.9)	293 433 (52.1)
Total	3 832 034 (100.0)	1 870 435 (48.8)	1 961 599 (51.2)

[a] The proportions of males and females in each ethnic group. *Compared with the other ethnic groups, the proportions of males were significantly higher in the Manchu population (all P<0.001).

Table 2. Distribution of ABO blood groups in the study population according to ethnicity

Ethnicity	Number	ABO phenotype (%)			
		A	B	AB	O
Han	3 473 527	1 065 599 (30.7)	1 021 051 (29.4)	338 230 (9.7)	1 048 647 (30.2)
Uygur	129 454	39 745 (30.7)	39 857 (30.8)	13 727 (10.6)*	36 125 (27.9)
Zhuang	47 305	11 917 (25.2)	13 006 (27.5)	2602 (5.5)	19 780 (41.8)*
Manchu	33 182	8438 (25.4)	11 180 (33.7)*	3132 (9.4)	10 432 (31.4)
Miao	27 637	7847 (28.4)	7435 (26.9)	1932 (7.0)	10 423 (37.7)*
Yi	19 659	6675 (34.0)*	5191 (26.4)	1778 (9.0)	6015 (30.6)
Mongolian	18 996	4983 (26.2)	6320 (33.3)*	1840 (9.7)	5853 (30.8)
Hui	11 471	3411 (29.7)	3429 (29.9)	1134 (9.9)	3497 (30.5)
Others	70 803	21 550 (30.4)	19 963 (28.2)	5887 (8.3)	23 403 (33.1)
Total	3 832 034	1 170 165 (30.5)	1 127 432 (29.4)	370 262 (9.7)	1 164 175 (30.4)

* Compared with the other ethnic groups, the proportions of group A (B, AB, or O) were all significantly higher (P<0.001).

Table 3. Distribution of RhD blood groups in the study population according to ethnicity

Ethnicity	Total	RhD–	
		N	Proportion (%, 95% CI)
Han	3 473 527	33 003	0.95 (0.94-0.96)
Uygur	129 454	4309	3.33 (3.23-3.43)[a]
Zhuang	47 305	240	0.51 (0.44-0.57)
Manchu	33 182	121	0.36 (0.30-0.43)
Miao	27 637	191	0.69 (0.59-0.79)
Yi	19 659	245	1.25 (1.09-1.40)
Mongolian	18 996	65	0.34 (0.26-0.43)
Hui	11 471	92	0.80 (0.64-0.97)
Others	70 803	739	1.04 (0.97-1.12)
Total	3 832 034	39 005	1.02 (1.01-1.03)

RhD–, RhD negative; CI, confidence interval; *, P<0.001.

[a] Compared with the other ethnic groups, the proportions of the RhD– group were significantly higher in the Uygur population (all P<0.001).

Table 4. Distribution of ABO and RhD blood groups in the study population according to ethnicity

Ethnicity	Number	Phenotype (%)							
		A RhD+	A RhD–	B RhD+	B RhD–	AB RhD+	AB RhD–	O RhD+	O RhD–
Han	3 473 527	1 053 849 (30.3)	11 750 (0.3)	1 011 421 (29.1)	9630 (0.3)	335 237 (9.7)	2993 (0.1)	1 040 017 (29.9)	8630 (0.3)
Uygur	129 454	38 265 (29.6)	1480 (1.1)	38 529 (29.8)	1328 (1.0)	13 307 (10.3)	420 (0.3)	35 044 (27.1)	1081 (0.8)
Zhuang	47 305	11 821 (25.0)	96 (0.2)	12 938 (27.4)	68 (0.1)	2594 (5.5)	8 (0.02)	19 712 (41.7)	68 (0.1)
Manchu	33 182	8396 (25.3)	42 (0.1)	11 138 (33.6)	42 (0.1)	3123 (9.4)	9 (0.03)	10 404 (31.6)	28 (0.1)
Miao	27 637	7786 (28.2)	61 (0.2)	7372 (26.7)	63 (0.2)	1920 (7.0)	12 (0.04)	10 368 (37.5)	55 (0.2)
Yi	19 659	6601 (33.6)	74 (0.4)	5119 (26.0)	72 (0.4)	1755 (8.9)	23 (0.1)	5939 (30.2)	76 (0.4)
Mongolian	18 996	4968 (26.2)	15 (0.1)	6295 (33.1)	25 (0.1)	1834 (9.7)	6 (0.03)	5834 (30.7)	19 (0.1)
Hui	11 471	3381 (29.5)	30 (0.3)	3398 (29.6)	31 (0.3)	1124 (9.8)	10 (0.1)	3476 (30.3)	21 (0.2)
Others	70 803	21 320 (30.1)	230 (0.3)	19 731 (27.9)	232 (0.3)	5803 (8.2)	84 (0.1)	23 210 (32.8)	193 (0.3)
Total	3 832 034	1 156 387 (30.2)	13 778 (0.4)	1 115 941 (29.1)	11 491 (0.3)	366 697 (9.6)	3565 (0.1)	1 154 004 (30.1)	10 171 (0.3)

RhD+ represents RhD positive, and RhD– represents RhD–.

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cross-sectional studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3
Objectives	3	State specific objectives, including any prespecified hypotheses	3
Methods			
Study design	4	Present key elements of study design early in the paper	3
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	3
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	3
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	4
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	3-4
Bias	9	Describe any efforts to address potential sources of bias	*4*
Study size	10	Explain how the study size was arrived at	3
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	4
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	4
		(*b*) Describe any methods used to examine subgroups and interactions	4
		(*c*) Explain how missing data were addressed	4
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	4
		(*e*) Describe any sensitivity analyses	Not applicable
Results			

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	4
		(b) Give reasons for non-participation at each stage	Not applicable
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	4
		(b) Indicate number of participants with missing data for each variable of interest	4
Outcome data	15*	Report numbers of outcome events or summary measures	4
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	4
		(*b*) Report category boundaries when continuous variables were categorized	4
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	Not applicable
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	5
Discussion			
Key results	18	Summarise key results with reference to study objectives	5-6
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	6
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	5-6
Generalisability	21	Discuss the generalisability (external validity) of the study results	6
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	7

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Frequencies and ethnic distribution of ABO and RhD blood groups in China: a population-based cross-sectional study

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Title page

Title: Frequencies and ethnic distribution of ABO and RhD blood groups in China: a population-based cross-sectional study

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Abbreviations: RhD–, RhD negative; RhD+, RhD positive; NFPHEP, National Free Preconception Health Examination Project; CI, confidence interval.

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Frequencies and ethnic distribution of ABO and RhD blood groups in China: a population-based cross-sectional study

Abstract

Objectives ABO and RhD blood groups are key factors affecting blood transfusion safety. The distribution of ABO and RhD blood groups varies globally, but limited data exist for ethnic distributions of these blood groups in Asian populations. We aimed to evaluate the distribution of ABO and RhD blood groups among Chinese ethnic groups.

Design A population-based cross-sectional study.

Setting Data on ABO groups and ethnicities were obtained from the National Free Preconception Health Examination Project (NFPHEP) with participants from 220 counties of 31 provinces in China

Participants There were 3 832 034 participants aged 21 to 49 years who took part in the NFPHEP from January 2010 and December 2012 and were included in this study.

Outcome Measures The proportion of ABO and RhD blood groups among different ethnic groups was calculated.

Results ABO and RhD blood distribution was significantly different among nine ethnic groups (P<0.001). Compared with other ethnic groups, the Yi group had more A phenotypes (34.0%), and the Manchu (33.7%) and Mongolian (33.3%) ethnic groups had more B phenotypes. The Zhuang group had the greatest proportion of O phenotypes (41.8%), followed by the Miao group (37.7%). AB phenotypes were more frequent in the Uygur ethnic group (10.6%) but lower in the Zhuang group (5.5%). Meanwhile, RhD negativity (RhD–) was greater in the Uygur group (3.3%) than in the Mongolian (0.3%) and Manchu ethnic groups (0.4%). O RhD– blood groups were more frequent in the Uygur group (0.8%) than in the other ethnic groups (0.1%–0.4%, P<0.001).

Conclusion ABO and RhD blood phenotypes vary across different ethnic groups in China. The diversity in the distribution of the ABO and RhD blood groups in different ethnic groups should be considered when developing rational and evidence-based strategies for blood collection and management.

Strengths and limitations of this study

- To our knowledge, this is the largest population-based study of ABO and RhD blood type distribution in different ethnic groups among the general population in an Asian country.
- A major limitation of the study was that there was no further laboratory data on the subtypes of the ABO blood groups (e.g. A1, A2, A3, Aw, Ax, and Ael).
- We did not assess all of the 55 ethnic minority groups in China, but we assessed the 7 ethnic minority groups with larger population sizes.
- Participants' willingness to donate and history of blood donation were not investigated, so we could not provide specific evidence on donor recruitment.

Introduction

ABO and RhD blood groups, the most well-known blood group systems, are of key importance for transfusion safety and clinical practice and are also thought to be linked with disease susceptibility [1, 2]. The distribution of ABO and RhD blood groups varies throughout the world;[3-5] previous studies have found the percentage of blood group O to be 46.6% in the United States[3], 34% in China[4], 49.10% in Mauritania[5], 38.9% in Sweden[6], and 42.3% in Denmark[6]. The proportion of those with RhD-negative (RhD–) blood has been reported to be 14.6% in the United States[3], 17.9% in Sweden and Denmark[6], and between 0.4%-1.0% in China[4]; this also varies among different races or ethnic populations.[3, 5, 7] In the United States, the percentage of group O varies from 39.8% in Asian donors to 56.5% in Hispanic donors, and the proportion of RhD– varies from 1.7% in Asian donors to 17.3% in White non-Hispanic donors.[3] Data regarding the distribution of ABO and RhD blood groups were primarily obtained from blood donors in previous studies, whilst little data came from the general population.

China comprises more than 20% of the world's population.[8] Social–economic development and increased health care coverage have increased the demand for blood and its products in China[9]. Despite steady increases in total blood collections and voluntary non-remunerated donors, China faces challenges to its blood donation system.[10] 9% of Chinese donate blood, and more than 60% of donors are first-time donors.[10] Thus, data regarding the frequencies and ethnic distributions of ABO and RhD blood groups in the general population may help us to develop rational and evidence-based strategies for blood collection and management. However, studies that focused on the frequency and ethnic distribution of ABO and RhD blood groups in the general population have been scarce in China.

Thus, we conducted a large population-based study to investigate the distribution of ABO and RhD blood groups in different ethnic groups in the general population in China to provide reliable data for better development of rational strategies for blood collection and management.

Materials and methods

Study design and data source

We performed a nationwide population-based, cross-sectional study using data from the National Free Preconception Health Examination Project (NFPHEP), which is a national health check-up program that offers free preconception health examinations and counseling services for married couples preparing for pregnancy. It was launched by the Chinese National Health and Family Planning Commission and the Ministry of Finance in 2010. Project-related design and implementation were previously described[11-14]. This study was approved by the Institutional Review Board of the Chinese Association of Maternal and Child Health Studies. All participants were provided with written informed consent forms before enrollment.

From January 1, 2010, to December 31, 2012, there were 4 150 214 participants (2 120 131 women and 2 030 083 men) aged 21–49 years from 220 counties in 31 provinces enrolled in the NFPHEP, covering 86.1% of the target population[15]. 318 180 (7.7%) participants who did not undergo ABO and RhD blood typing were excluded, yielding 3 832 034 enrolled participants who were included for analysis.

Questionnaire and laboratory testing

Basic information was collected by trained local health workers from all of the participants in the

NFPHEP using a standardized questionnaire that inquired about gender, age, educational level, occupation, address of residence, and ethnicity (Han, Uygur, Zhuang, Manchu, Miao, Yi, Mongolian, Hui, or Others). Information on ethnicity was collected based on identification card of the participants to avoid recall bias. During the physical examination, trained local health workers collected blood samples from all of the participants and immediately sent them to local laboratories. Testing for both the ABO and RhD blood groupings was performed simultaneously with reagents (anti-A, anti-B, anti-AB, and anti-D). The red blood cell agglutination method was used for blood type analysis. The National Center of Clinical Laboratories for Quality Inspection and Detection performed a biannual external quality assessment for quality control.

Statistical analysis

We used proportions to describe distributions of gender, age, ethnicity and other socio-demographic characteristics of the participants. We used Chi-square tests to compare proportions of A, B, AB and O blood groups across ethnicities. The proportion of RhD– and its 95% confidence interval (CI) was calculated. The Chi-square test was also used to compare the proportion of RhD– blood groups across ethnicities. According to the ABO phenotypes (A, B, AB, and O) and RhD phenotypes (RhD– and RhD+), we divided the participants into 8 blood groups, namely A RhD+, A RhD–, B RhD+, B RhD–, AB RhD+, AB RhD–, O RhD+ and O RhD–. We used the Chi-square test to compare distributions of ABO/RhD phenotypes across ethnicities. All of the analyses were done with SPSS version 18.0 (SPSS Inc., Chicago, IL, USA). Two-sided $p < 0.05$ was considered to be statistically significant.

Results

Demographic characteristics of the study population

Of the 3 832 034 participants included in the study, 48.8% were male, 36.3% were older than 30 years of age. There were 3 473 527 (90.6%) of the participants who were of the Han ethnicity. The proportions of the Uygur, Zhuang, Manchu, Miao, Yi, Mongolian and Hui ethnicities were 3.4%, 1.2%, 0.9%, 0.7%, 0.5%, 0.5% and 0.3%, respectively (Table 1). The Manchu ethnic group (51.2%) had a significantly higher proportion of male proportion than other ethnicities (all $P < 0.001$).

Distribution of ABO blood groups according to ethnicity

In the ABO blood system, blood group A (30.5%) appeared to be the most common phenotype, followed by O (30.4%), B (29.4%), and AB (9.7%). The proportions of the A, B, O, and AB blood groups were significantly different among the 9 ethnic groups (all $P < 0.001$, Table 2). Compared with the other ethnic groups, the Yi ethnic group had a significantly higher proportion of the A phenotype (34.0%), while Manchu (33.7%) and Mongolian (33.3%) ethnic groups had a significantly higher proportion of the B phenotype (all $P < 0.001$). The Zhuang ethnic group had the highest proportion of the O phenotype (41.8%), followed by the Miao ethnic group (37.7%). The proportion of the AB phenotype was significantly higher in the Uygur ethnic group (10.6%) but lower in the Zhuang ethnic group (5.5%, all $P < 0.001$).

Distribution of RhD blood groups according to ethnicity

In the Rh blood system, 1.02% (95% CI: 1.01-1.03) of the 3 832 034 participants were RhD– (Table 3). The proportion of the RhD– group was significantly different among the 9 ethnic groups ($\chi^2 = 7413.07$, $P<0.001$). Compared with other ethnic groups, the proportion of RhD– appeared to be significantly higher in the Uygur ethnic group (3.3%), while much lower in the Mongolian (0.3%)

and Manchu ethnic groups (0.4%). The proportion of RhD– in the Yi (1.25%), Han (0.95%), and other ethnic groups (1.04%) was significantly different from each other (all P < 0.01). Compared with the Han ethnic group, participants of Uygur ethnicity (OR=3.59; 95% CI, 3.48-3.71), Yi ethnicity (OR=1.32; 95% CI, 1.16-1.49), and others (OR=1.10; 95% CI, 1.02-1.18) all had a significantly higher proportion of RhD–.

Distribution of ABO and RhD blood groups according to ethnicity

Compared with other ethnic groups, the Yi group had more A RhD+ phenotypes (33.6%), and the Uygur group had more A RhD– phenotypes (1.1%, all P < 0.001). O RhD– blood groups were more frequent in the Uygur group (0.8%) than in the other ethnic groups (0.1%–0.4%, P < 0.001). O RhD+ blood groups were frequent in the Zhuang group (41.7%) than in other ethnic groups (27.1%-37.5%, P < 0.001). The proportions of AB RhD+ blood group (10.3%) and AB RhD– blood group (0.3%) were both higher in the Uygur than in other ethnic groups (all P < 0.001). The distribution of ABO and RhD combination phenotypes across ethnicities is shown in Table 4.

Discussion

Similar with other developing countries, China has made progress on blood safety and availability through persistent efforts on blood screening and supply in the past decades.[16] China has 452 blood banks and 32 blood centers nationwide, but still faces challenges in limited donors and blood shortage.[16] How ABO/RhD blood groups are distributed in the general population is of interest to improve blood services.

In this population-based study involving 3.8 million adults in China, we found that the A phenotype was the most common, followed by the O, B and AB phenotypes; O phenotype was more frequent in the Zhuang group; and RhD– phenotype was more frequent in the Uygur group. Zu and colleagues[17] reported A, O, B, and AB phenotypes to be 31.9%, 31.0%, 28.1%, and 9.1%, respectively, in 19 247 patients without congenital heart disease in China, which were similar with our findings. This was a general population of patients without heart disease, therefore the data matches closely to our study conducted as there were likely to be all ethnicities present. In the Chinese blood donors, Guo and colleagues[4] reported that O phenotype was the most frequent (34.0%) and RhD– phenotype was 1.0% among 512,594 donations at 5 blood centers in China. Different characteristics between general population and blood donors might contribute to the discrepancy on ABO distribution, because it was found that Han donors were under-represented (86.2%) compared to the general population (>90%).[4] Li and colleagues[18] found that RhD- donors were more prevalent especially from the Uygur population (5%), which was consistent with the findings from the general population. However, these numbers are much lower than data (17.9% for RhD- phenotype) from Sweden and Denmark.[6] In the United States, Garratty and colleagues[3] demonstrated that percentages of group O were 39.8% in Asian donors, 56.5% in Hispanic donors and 54.6% in North American Indian donors. And they found that the proportions of RhD– was much lower in Asian donors (1.7%) than that in White non-Hispanic donors (17.3%) and North American Indian donors (9.7%).[3] The ABO and RhD blood phenotypes vary widely across races/ethnicities and geographical boundaries.[3, 19] These findings highlight that it is necessary to consider ethnic diversity when developing recruitment strategies.

The majority of the population in China are of Han ethnicity (91.6%) and the minority of the population are of the other 55 ethnicities (8.4%), according to the Sixth National Population Census Report.[20] The Distribution of ethnic groups in our study was similar to this report. The

Zhuang, Manchu, Uygur, Miao, Yi, Hui, and Mongolian populations were assessed in our study; they are the top seven ethnic groups among the 55 minorities. In China, whole blood collection has increased rapidly over the past decade, from 6.75 million donations in 2006 to 12.32 million donations in 2011; however, it is still far from the ever-increasing demand.[9, 21] Our findings on the ethnic diversity of blood group distribution would be helpful to design better recruitment strategies to prevent blood shortages.

Take group O RhD– for example, it is well-known that group O RhD– is a precious resource that are often in short supply.[22] Studies have shown that supplying the "universal" O RhD– blood group on time and on demand to hospitals is an ongoing challenge.[22-24] Hirani and colleagues.[23] showed that, as patient blood management became more widespread, there was an international decline in the demand for red blood cell units with a 21% reduction between 2012 and 2015 in Australia.[23] On the contrary, the demand for the O RhD– blood group was in fact proportionally increasing. [23,24] A significant proportion of O RhD– blood units were transfused to compatible, non-identical recipients, although the frequency of this practice varied across sites from 0% to 33% in Australia.[22] The transfusion of group O RhD– blood to non-O RhD+ recipients can result in shortages of group O RhD– blood. Interestingly, we found that the majority of the population was RhD+ and only 0.3% were O RhD– blood in the Chinese general population. Given the high proportion of RhD+, the likelihood of emergency/trauma patients being RhD- and therefore susceptible to alloimmunization are so remote that collections of O RhD+ might be more sensible. Studies have showed that transfusing emergency patients with unknown blood type with O RhD+ red blood cell concentrates has a low risk of inducing anti-D antibodies (3%-7%).[25-26] RhD- blood types may not be as vitally required in China as in other countries with high proportion of RhD- blood. Information on the distribution of the O RhD+ and O RhD- blood groups in different ethnic groups is of importance for developing better rational strategies for blood collection and management in China, especially during blood shortages.

ABO and RhD blood groups are reported to be associated with many diseases.[1, 2] Understanding the distribution of blood groups in the general population can provide information on the potential risk of diseases based on their blood groups. Zu and colleagues.[17] evaluated the relationship between the ABO blood group and congenital heart disease in 39 042 consecutive inpatients in a 6-year cohort study and found that the A blood group demonstrated a decreased risk for isolated congenital heart disease (odds ratio 0.82; 95% CI, 0.78-0.87). Amundadottir and colleagues.[27] conducted a two-stage genome-wide association study and identified an association between the ABO blood group gene and pancreatic cancer. Genetic traits might contribute to the link between ABO and RhD blood groups and disease susceptibility, and contribute to the diverse distribution of ABO and RhD blood groups in different ethnic groups as well.

To our knowledge, this is the largest population-based study of ABO and RhD blood type distributions across ethnicities in China. However, there were several limitations in our study. First, information on the subtypes of the ABO blood groups (e.g. A1, A2, A3, Aw, Ax, and Ael) was not available in the NFPHEP, thus the distribution of those ABO subtypes could not further be assessed. Second, we did not assess all of the 55 ethnic minorities in China. Nevertheless, we assessed 7 minorities with a large-sized population. Third, donor willingness and histories of blood donation were not investigated in the NFPHEP, so we could not provide specific evidence on donor recruitment.

In conclusion, ABO and RhD blood phenotypes varied across ethnicities in China. Diversity in

the distribution of the ABO and RhD blood groups in different ethnic groups should be considered when developing rational and evidence-based strategies for blood collection and management. Our data should allow targeted donor management to increase the proportion of needed blood type products, especially for blood types that are high in demand but low in supply.

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Contributors: JL and SZ searched the literature, designed the study, analyzed the data, interpreted the results, and drafted the manuscript. QW, HS and YZ collected the data and revised the manuscript. ML conceived the study, designed the study, supervised the study, interpreted the results, and revised the manuscript. All authors have read and approved the final manuscript. ML is the study guarantors. ML has the right to grant on behalf of all authors and does grant on behalf of all authors.

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Provenance and peer review Not commissioned; externally peer reviewed.

Data sharing statement: Due to privacy and ethical concerns, supporting data cannot be made openly available. Please contact the authors for the access of the original data.

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Table 1. Socio-demographic characteristics of the study population

Characteristic	Total (%)	Male (%)[a]	Female (%)[a]
Ethnicity			
Han	3473527 (90.6)	1 698 090 (48.9)	1 775 437 (51.1)
Uygur	129454 (3.4)	64 559 (49.9)	64 895 (50.1)
Zhuang	47305 (1.2)	22 735 (48.1)	24 570 (51.9)
Manchu	33182 (0.9)	16 988 (51.2)*	16 194 (48.8)
Miao	27637 (0.7)	12 212 (44.2)	15 425 (55.8)
Yi	19659 (0.5)	8839 (45.0)	10 820 (55.0)
Mongolian	18996 (0.5)	9148 (48.2)	9848 (51.8)
Hui	11471 (0.3)	5588 (48.7)	5883 (51.3)
Others	70803 (1.8)	32 276 (45.6)	38 527 (54.4)
Age (years)			
21-29	2 405 744 (62.8)	1 035 243 (43.0)	1 370 501 (57.0)
30-39	1 247 194 (32.5)	723 523 (58.0)	523 671 (42.0)
40-49	179 096 (4.7)	111 669 (62.4)	67 427 (37.6)
Region			
Eastern	857 763 (22.4)	416 191 (48.5)	441 572 (51.5)
Central	1 930 145 (50.4)	945 877 (49.0)	984 268 (51.0)
Western	1 044 126 (27.2)	508 367 (48.7)	535 759 (51.3)
Education			
Primary school or below	178 680 (4.7)	80 321 (45.0)	98 359 (55.0)
Junior high school	2 503 844 (65.3)	1 202 193 (48.0)	1 301 651 (52.0)
Senior high school	700 159 (18.3)	358 423 (51.2)	341 736 (48.8)
College or higher	449 351 (11.7)	229 498 (51.1)	219 853 (48.9)
Occupation			
Farmers	2 914 777 (76.1)	1 403 135 (48.1)	1 511 642 (51.9)
Factory workers	354 080 (9.2)	197 556 (55.8)	156 524 (44.2)
Others	563 177 (14.7)	269 744 (47.9)	293 433 (52.1)
Total	3 832 034 (100.0)	1 870 435 (48.8)	1 961 599 (51.2)

[a] The proportions of males and females in each ethnic group. *Compared with the other ethnic groups, the proportions of males were significantly higher in the Manchu population (all P<0.001).

Table 2. Distribution of ABO blood groups in the study population according to ethnicity

Ethnicity	Number	ABO phenotype (%)			
		A	B	AB	O
Han	3 473 527	1 065 599 (30.7)	1 021 051 (29.4)	338 230 (9.7)	1 048 647 (30.2)
Uygur	129 454	39 745 (30.7)	39 857 (30.8)	13 727 (10.6)*	36 125 (27.9)
Zhuang	47 305	11 917 (25.2)	13 006 (27.5)	2602 (5.5)	19 780 (41.8)*
Manchu	33 182	8438 (25.4)	11 180 (33.7)*	3132 (9.4)	10 432 (31.4)
Miao	27 637	7847 (28.4)	7435 (26.9)	1932 (7.0)	10 423 (37.7)*
Yi	19 659	6675 (34.0)*	5191 (26.4)	1778 (9.0)	6015 (30.6)
Mongolian	18 996	4983 (26.2)	6320 (33.3)*	1840 (9.7)	5853 (30.8)
Hui	11 471	3411 (29.7)	3429 (29.9)	1134 (9.9)	3497 (30.5)
Others	70 803	21 550 (30.4)	19 963 (28.2)	5887 (8.3)	23 403 (33.1)
Total	3 832 034	1 170 165 (30.5)	1 127 432 (29.4)	370 262 (9.7)	1 164 175 (30.4)

* Compared with the other ethnic groups, the proportions of group A (B, AB, or O) were all significantly higher (P<0.001).

Table 3. Distribution of RhD blood groups in the study population according to ethnicity

Ethnicity	Total	RhD–	
		N	Proportion (%, 95% CI)
Han	3 473 527	33 003	0.95 (0.94-0.96)
Uygur	129 454	4309	3.33 (3.23-3.43)*
Zhuang	47 305	240	0.51 (0.44-0.57)
Manchu	33 182	121	0.36 (0.30-0.43)
Miao	27 637	191	0.69 (0.59-0.79)
Yi	19 659	245	1.25 (1.09-1.40)
Mongolian	18 996	65	0.34 (0.26-0.43)
Hui	11 471	92	0.80 (0.64-0.97)
Others	70 803	739	1.04 (0.97-1.12)
Total	3 832 034	39 005	1.02 (1.01-1.03)

RhD–, RhD negative; CI, confidence interval;

*Compared with the other ethnic groups, the proportions of the RhD– group were significantly higher in the Uygur population (all P<0.001).

Table 4. Distribution of ABO and RhD blood groups in the study population according to ethnicity

Ethnicity	Number	Phenotype (%)							
		A RhD+	A RhD–	B RhD+	B RhD–	AB RhD+	AB RhD–	O RhD+	O RhD–
Han	3 473 527	1 053 849 (30.3)	11 750 (0.3)	1 011 421 (29.1)	9630 (0.3)	335 237 (9.7)	2993 (0.1)	1 040 017 (29.9)	8630 (0.3)
Uygur	129 454	38 265 (29.6)	1480 (1.1)	38 529 (29.8)	1328 (1.0)	13 307 (10.3)	420 (0.3)	35 044 (27.1)	1081 (0.8)
Zhuang	47 305	11 821 (25.0)	96 (0.2)	12 938 (27.4)	68 (0.1)	2594 (5.5)	8 (0.02)	19 712 (41.7)	68 (0.1)
Manchu	33 182	8396 (25.3)	42 (0.1)	11 138 (33.6)	42 (0.1)	3123 (9.4)	9 (0.03)	10 404 (31.6)	28 (0.1)
Miao	27 637	7786 (28.2)	61 (0.2)	7372 (26.7)	63 (0.2)	1920 (7.0)	12 (0.04)	10 368 (37.5)	55 (0.2)
Yi	19 659	6601 (33.6)	74 (0.4)	5119 (26.0)	72 (0.4)	1755 (8.9)	23 (0.1)	5939 (30.2)	76 (0.4)
Mongolian	18 996	4968 (26.2)	15 (0.1)	6295 (33.1)	25 (0.1)	1834 (9.7)	6 (0.03)	5834 (30.7)	19 (0.1)
Hui	11 471	3381 (29.5)	30 (0.3)	3398 (29.6)	31 (0.3)	1124 (9.8)	10 (0.1)	3476 (30.3)	21 (0.2)
Others	70 803	21 320 (30.1)	230 (0.3)	19 731 (27.9)	232 (0.3)	5803 (8.2)	84 (0.1)	23 210 (32.8)	193 (0.3)
Total	3 832 034	1 156 387 (30.2)	13 778 (0.4)	1 115 941 (29.1)	11 491 (0.3)	366 697 (9.6)	3565 (0.1)	1 154 004 (30.1)	10 171 (0.3)

RhD+ represents RhD positive, and RhD– represents RhD negative.

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cross-sectional studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3
Objectives	3	State specific objectives, including any prespecified hypotheses	3
Methods			
Study design	4	Present key elements of study design early in the paper	3
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	3
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	3
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	4
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	3-4
Bias	9	Describe any efforts to address potential sources of bias	*4*
Study size	10	Explain how the study size was arrived at	3
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	4
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	4
		(*b*) Describe any methods used to examine subgroups and interactions	4
		(*c*) Explain how missing data were addressed	4
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	4
		(*e*) Describe any sensitivity analyses	NA
Results			

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	4
		(b) Give reasons for non-participation at each stage	3
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	4
		(b) Indicate number of participants with missing data for each variable of interest	4
Outcome data	15*	Report numbers of outcome events or summary measures	4
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	4
		(*b*) Report category boundaries when continuous variables were categorized	4
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	NA
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	5
Discussion			
Key results	18	Summarise key results with reference to study objectives	5-6
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	6
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	5-6
Generalisability	21	Discuss the generalisability (external validity) of the study results	6
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	7

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.